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(54) Title: METHOD

(57) Abstract: The invention relates to a method of selecting a mammal having or suspected of having a tumour for treatment with an erbB receptor drug which comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 1 or 2 as defined herein whereby to predict an increased likelihood of response to the erbB receptor drug. Preferred genes include any one of NES, GSPT2, ETR101, TAZ, CHST7, DNAJC3, NPAS2, PIN1, TCEA2, VAMP4, DAPK1, DAPK2, MLLT3, TNNC1, KIAA0931, ACOX2, EMP1, SLC20A1, SPRY2 or PGM1.

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METHOD

The present invention relates to sensitivity of tumours to therapeutic agents which can be predicted from the gene expression profile of the tumour and hence that the suitability of cancer patients for treatment with such therapeutic agents can be determined by measuring the relative expression levels of particular genes in tumour tissue.

The phosphorylation of proteins on tyrosine residues is a key element of signal transduction within cells. Enzymes capable of catalysing such reactions are termed tyrosine kinases. A number of these enzymes exist as integral components of transmembrane receptor molecules and are classified as receptor tyrosine kinases (RTKs). There are several members of this family of RTKs, class I of which includes the erbB family, e.g. epidermal growth factor receptor (EGFR), erbB2, erbB3 and erbB4. Binding of a variety of ligands to the external domain activates the EGFR tyrosine kinase domain. Activation causes EGFR itself and a number of cellular substrates to become phosphorylated on tyrosine residues. These phosphorylation reactions are a major component of growth factor induced proliferation of cells.

The erbB family of receptor tyrosine kinases are known to be frequently involved in driving the proliferation and survival of tumour cells (reviewed in Olayioye *et al.*, *EMBO J.*, 2000, 19, 3159). One mechanism by which this can occur is over expression of the receptor at the protein level, for example as a result of gene amplification. This has been observed in many common human cancers (reviewed in Klapper *et al.*, *Adv. Cancer Res.*, 2000, 77, 25) such as, non-small cell lung cancers (NSCLCs) including adenocarcinomas (Cerny *et al.*, *Brit. J. Cancer*, 1986, 54, 265; Reubi *et al.*, *Int. J. Cancer*, 1990, 45, 269; Rusch *et al.*, *Cancer Research*, 1993, 53, 2379; Brabender *et al.*, *Clin. Cancer Res.*, 2001, 7, 1850) as well as other cancers of the lung (Hendler *et al.*, *Cancer Cells*, 1989, 7, 347).

It is now several decades since the study of retroviral mediated cellular transformation began to revolutionize our understanding of malignant transformation. Transformation was shown to be dependent on oncogenes carried by viruses and these were shown to have mammalian cellular counterparts, proto-oncogenes. In 1984, EGFR was described as the mammalian counterpart of the retroviral oncogene, v-erbB (Downward *et al.*). This, coupled to earlier observations describing a two component autocrine growth promoting mechanism in cancer cells consisting of EGF ligand and its receptor EGFR (Sporn & Todaro), strengthened

the hypothesis that EGFR signalling is an important contributor to tumourigenesis. Subsequent reports continued to provide evidence that EGFR is an attractive target for therapeutic intervention in Cancer (see Yarden & Slivkowski for review). EGFR is markedly overexpressed across a large variety of epithelial Cancers (see Salomon et al) and some immunohistochemical studies have demonstrated EGFR expression is associated with poor prognosis. In addition to overexpression, it is recognised that there is potential for deregulated EGFR signalling in tumours via a number of alternative mechanisms including i) EGFR mutations ii) increased ligand expression and enhanced autocrine loop and iii) heterodimerisation and cross talk with other erbB receptor family members.

In addition, a wealth of pre-clinical information suggests that the erbB family of receptor tyrosine kinases are involved in cellular transformation. In addition to this, a number of pre-clinical studies have demonstrated that anti-proliferative effects can be induced by knocking out one or more erbB activities by small molecule inhibitors, dominant negatives or inhibitory antibodies (reviewed in Mendelsohn et al., Oncogene, 2000, 19, 6550).

Thus it has been recognised that inhibitors of these receptor tyrosine kinases should be of value as a selective inhibitor of mammalian cancer cells (Yaish et al. Science, 1988, 242, 933, Kolibaba et al, Biochimica et Biophysica Acta, 1997, 133, F217-F248; Al-Obeidi et al, 2000, Oncogene, 19, 5690-5701; Mendelsohn et al, 2000, Oncogene, 19, 6550-6565).

A number of small molecule inhibitors of erbB family of receptor tyrosine kinases are known, particularly inhibitors of EGF and erbB2 receptor tyrosine kinases. For example European Patent Application No. 0566226 and International Patent Applications WO 96/33980 and WO 97/30034 disclose that certain quinazoline derivatives which possess an anilino substituent at the 4-position possess EGFR tyrosine kinase inhibitory activity and are inhibitors of cancer tissue.

It has been disclosed by J R Woodburn et al. in Proc. Amer. Assoc. Cancer Research, 1997, 38, 633 and Pharmacol. Ther., 1999, 82, 241-250 that the compound N-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine is a potent EGFR tyrosine kinase inhibitor. This compound is also known as Iressa (registered trade mark), gefitinib (United States Adopted Name), by way of the code number ZD1839 and Chemical Abstracts Registry Number 184475-35-2. The compound is principally identified hereinafter as gefitinib.

Gefitinib was developed as an inhibitor of epidermal growth factor receptor-tyrosine kinase (EGFR-TK), which blocks signalling pathways responsible for driving proliferation, invasion, and survival of cancer cells (Wakeling, A.E., et al. *Cancer Res*, 2002, 62(20), p5749). Gefitinib has provided clinical validation of small molecule inhibitors of EGFR. Potent anti-tumour effects as well as rapid improvements in NSCLC-related symptoms and quality of life have been observed in clinical studies that enrolled patients with advanced NSCLC who did not respond to platinum-based chemotherapy. The Phase II 'IDEAL' trials demonstrated that single agent gefitinib resulted in objective anti-tumour activity, symptomatic improvement and limited toxicity in patients with advanced NSCLC and previously treated with cytotoxic chemotherapy (Fukuoka et al., Kris et al). Objective response rate (Complete Response + Partial Response) was 18.4% and 11.8% respectively in the IDEAL 1 and IDEAL 2 trials. The differences in response in these clinical trials has been attributed to different population groups in the two trials, predominantly Japanese in IDEAL 1 and a predominantly European-derived population in IDEAL 2. Beyond objective responses, additional patients experienced stable disease and / or symptom improvement meaning that approximately 50% of patients overall benefit from gefitinib. The tumour response data has been the basis of initial regulatory approvals of gefitinib in advanced NSCLC in several markets.

It is important to be able to understand the basis of response to anti-cancer therapeutic agents such as gefitinib since this would allow clinicians to maximise the benefit/risk ratio for each patient, potentially via the development of diagnostic tests to identify patients most likely to benefit from gefitinib treatment. An obvious candidate marker of response to gefitinib has been EGFR expression level. However, gefitinib inhibition of growth of some cancer-derived cell lines and tumour xenografts is not well correlated with the level of expression of EGFR. Furthermore, studies alongside the IDEAL trials demonstrated that EGFR protein expression as measured by IHC was not an accurate predictor of response to gefitinib (Bailey et al). Although there are now several additional hypotheses based on genetics, genomics, proteomics, biochemical and other studies, there is still no pre-treatment predictive biomarker of gefitinib response currently approved by regulatory authorities. Possibly the most significant recent breakthrough in understanding gefitinib response has come from recent data (Lynch et al, Paez et al) indicating that mutation in the EGFR kinase domain predicts gefitinib hypersensitivity in NSCLC patients. Hypersensitivity is a vague term but in this field is generally understood to mean patients experiencing objective tumour responses (i.e. marked tumour regression,

normally above 50%). As well as demonstrating the EGFR mechanism of action for gefitinib, this may provide a basis for venturing into other disease settings such as first line, adjuvant and possibly earlier cancer intervention with EGFR inhibitors in a targeted subpopulation in NSCLC patients and other types of cancers carrying the EGFR mutation.

However, it is likely that restricting prescription of gefitinib to the mutant EGFR carrying tumour subgroup will deprive many patients who could benefit from gefitinib. Firstly there are emerging reports of gefitinib hypersensitive patients with undetectable EGFR mutation in their tumour and other patients with EGFR mutation who do not respond to gefitinib. Secondly, data reported at ASCO 2004 (Shepherd et al) indicated that the EGFR small molecule tyrosine kinase inhibitor erlotinib (Roche, Genentech, OSI) prolongs survival in advanced NSCLC previously treated with chemotherapy, by ~2 months across the population with resulting 41% reduction in risk of death at one year. Most interestingly, the survival benefit appears to be derived from patients in the stable disease response population as well as hypersensitive patients. This highlights the likely importance of identifying likely gefitinib responsive patients beyond those carrying EGFR mutation. Definitive survival benefit is also likely to be demonstrated from ongoing clinical trials with gefitinib.

The differential response of patients to chemotherapy treatments indicates that there is a need to find methods of predicting which treatment regimes best suit a particular patient.

There is an increasing body of evidence that suggests that patients' responses to numerous drugs may be related to a patients' genetic, genomic, proteomic, biochemical or profile and that determination of the genetic factors that influence, for example, response to a particular drug could be used to provide a patient with a personalised treatment regime. Such personalised treatment regimes offer the potential to maximise therapeutic benefit to the patient, whilst minimising, for example side effects that may be associated with alternative and less effective treatment regimes.

Therefore there is a need for methods that can predict a patients' response to a drug based on the results of a test that indicates whether the patient is likely to respond to treatment or to be resistant to treatment.

The present invention is based on the discovery that the sensitivity of tumours to therapeutic agents can be predicted from the gene expression profile of the tumour and hence that the suitability of tumour patients for treatment with such therapeutic agents can be determined by measuring the relative expression levels of particular genes in tumour tissue.

According to one aspect of the present invention there is provided a method of selecting a mammal having or suspected of having a tumour for treatment with an erbB receptor drug which comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 1 as defined herein whereby to predict an increased likelihood of response to the erbB receptor drug.

According to another aspect of the present invention there is provided a method of selecting a mammal having or suspected of having a tumour for treatment with an erbB receptor drug which comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 1 or DAPK2 whereby to predict an increased likelihood of response to the erbB receptor drug.

In one embodiment the method comprises testing a biological sample from the mammal for expression of any one of ACOX2, NPAS2, NES, CHST7, GSPT2, DAPK1, DAPK2 or TNNC1. More preferably the method comprises testing a biological sample from the mammal for expression of any one of NPAS2, NES, CHST7 or DAPK1. More preferably the method comprises testing a biological sample from the mammal for expression of at least two of NPAS2, NES, CHST7 or DAPK1. More preferably the method comprises testing a biological sample from the mammal for expression of at least three of NPAS2, NES, CHST7 or DAPK1. More preferably still the method comprises testing a biological sample from the mammal for expression of NPAS2, NES, CHST7 and DAPK1.

In an alternative embodiment the method comprises testing a biological sample from the mammal for expression of any one of NES, GSPT2, ETR101, TAZ, CHST7, DNAJC3, NPAS2, PIN1, TCEA2, VAMP4, DAPK1, DAPK2, MLLT3, TNNC1 or KIAA0931. More preferably the method comprises testing a biological sample from the mammal for expression of any one of DAPK1, DAPK2 or NES. More preferably the method comprises testing a biological sample from the mammal for expression of at least two of DAPK1, DAPK2 or NES. More preferably the method comprises testing a biological sample from the mammal for expression of DAPK1, DAPK2 and NES.

In a preferred embodiment the method additionally comprises testing a biological sample from the mammal for expression of any gene listed in Table 2 as defined herein. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1, SLC20A1, SPRY2 or PGM1. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1.

In an alternative preferred embodiment the method additionally comprises testing a biological sample from the mammal for expression of any gene listed in Table 2 as defined herein. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1, HCA127, UBL5, ZNF23, UROD, CD44, SPRY1, RAPGEF2, SLC20A1, NRP1, PGM1, SPRY2, PTGER3, SCN10A, KITLG, CDH1, HOP, BCL3 or OLFM1. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1.

Preferably the tumour is selected from the group consisting of leukaemia, multiple myeloma, lymphoma, bile duct, bone, bladder, brain, CNS, glioblastoma, breast, colorectal, cervical, endometrial, gastric, head, neck, hepatic, lung, muscle, neuronal, oesophageal, ovarian, pancreatic, pleural membrane, peritoneal membrane, prostate, renal, skin, testicular, thyroid, uterine and vulval. More preferably the tumour is selected from one of non-small cell lung, pancreatic, head or neck. More preferably the tumour is selected from one of non-small cell lung, head or neck.

Preferably the erbB receptor drug is selected from any one of gefitinib, erlotinib, PKI-166, EKB-569, HKI-272, lapatinib, canertinib, ABE788, XL647, BMS 5599626, cetuximab, matuzumab, panitumumab, MR1-1, IMC-11F8 or EGFR11. Most preferably the erbB receptor drug is gefitinib.

In a further preferred embodiment of the method of the invention the mammal is a human and the method comprises testing a biological sample from the human for increased expression of DAPK1 and decreased expression of NPAS2, NES, CHST7 or EMP1 whereby to predict an increased likelihood of response to gefitinib. In an alternative preferred embodiment of the method of the invention the mammal is a human and the method comprises testing a biological sample from the human for increased expression of DAPK1 and DAPK2 and decreased expression of NES and EMP1 whereby to predict an increased likelihood of response to gefitinib.

According to another aspect of the invention there is provided an isolated set of marker genes identified as having differential expression between tumour cells that are sensitive and resistant to an erbB receptor drug said gene set comprising one or more genes selected from at least the group consisting of the genes listed in Table 1 defined herein or DAPK2, including gene specific oligonucleotides derived from said genes. Preferably the set comprises at least 2

genes, more preferably at least 3 genes, more preferably at least 4 genes. More preferably the set comprises at least one gene selected from Table 2 as defined herein.

According to another aspect of the invention there is provided an isolated set of marker genes identified as having differential expression between tumour cells that are sensitive and resistant to an erbB receptor drug said gene set comprising one or more genes selected from at least the group consisting of the genes listed in Table 1 defined herein, including gene specific oligonucleotides derived from said genes. Preferably the set comprises at least 2 genes, more preferably at least 3 genes. More preferably the set comprises at least one gene selected from Table 2 as defined herein.

The present invention permits the improved selection of a patient, having or suspected of having a tumour, for treatment with an erbB receptor drug, in order to predict an increased likelihood of response to the erbB receptor drug.

In one embodiment, the method comprises testing a biological sample from the mammal for expression of at least one or more of the following from Table 1, which are found at lower levels in sensitive cells NPAS2, NES, CHST7, ACOX2 or GSPT2 or at least one or more of the following which are found at higher levels in sensitive cells DAPK1 or TNNC1. The Affymetrix ID and Affymetrix probe sequence for these genes are displayed in Table 1. In a preferred embodiment, the method further comprises testing a biological sample from the mammal for expression of DAPK2 which is found at higher levels in sensitive cells, whereby to predict an increased likelihood of response to the erbB receptor drug.

In an alternative embodiment, the method comprises testing a biological sample from the mammal for expression of at least one or more of the following from Table 1, which are found at lower levels in sensitive cells NES, GSPT2, ETR101, TAZ, CHST7, DNAJC3, NPAS2, PIN1, TCEA2 or VAMP4 or at least one or more of the following which are found at higher levels in sensitive cells DAPK1, DAPK2, MLLT3, TNNC1 or KIAA0931. The Affymetrix ID and Affymetrix probe sequence for these genes are displayed in Table 1.

In a preferred embodiment, the method further comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 2, whereby to predict an increased likelihood of response to the erbB receptor drug. In a preferred embodiment, the method comprises testing a biological sample from the mammal for expression of any one of the following genes listed in Table 2, which are found at lower levels in sensitive cells EMP1, SLC20A1, SPRY2 or PGM1, whereby to predict an increased likelihood of response to the

erbB receptor drug. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1.

In an alternative preferred embodiment, the method further comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 2, whereby to predict an increased likelihood of response to the erbB receptor drug. In a preferred embodiment, the method comprises testing a biological sample from the mammal for expression of any one of the following genes listed in Table 2, which are found at lower levels in sensitive cells EMP1, HCA127, UBL5, ZNF23, UROD, CD44, SPRY1, RAPGEF2, SLC20A1, NRP1, PGM1 or SPRY2 or at least one or more of the following which are found at higher levels in sensitive cells PTGER3, SCN10A, KITLG, CDH1, HOP, BCL3 or OLFM1 whereby to predict an increased likelihood of response to the erbB receptor drug. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1.

In an especially preferred embodiment the method comprises testing a biological sample from the mammal for expression of NPAS2, NES, CHST7, DAPK1 and EMP1. High NPAS2, NES, CHST7 and EMP1 levels are associated with resistance to gefitinib and high DAPK1 levels are associated with sensitivity to gefitinib. Preferably, the assessment of expression comprises determination of whether DAPK1 levels are increased and NPAS2, NES, CHST7 and EMP1 levels are reduced.

In an alternative especially preferred embodiment the method comprises testing a biological sample from the mammal for expression of DAPK1, DAPK2, NES and EMP1. High EMP1 and NES levels are associated with resistance to gefitinib and high DAPK1 and DAPK2 levels are associated with sensitivity to gefitinib. Preferably, the assessment of expression comprises determination of whether DAPK1 and DAPK2 levels are increased and EMP1 and NES levels are reduced. In a most preferred embodiment the invention comprises determining the level of DAPK1 and EMP1.

According to another aspect of the invention there is provided a method for predicting clinical outcome of treatment with an erbB receptor drug for a mammal, having or suspected of having a tumour, comprising determining the level of any of the genes as described hereinabove in a biological sample taken from the tumour, or suspected tumour, wherein a poor outcome is predicted if:

- a) the expression level of DAPK1 is reduced; and /or

- b) the expression level of NPAS2, NES, CHST7 and EMP1 is increased.

According to another aspect of the invention there is provided a method for classifying cancer comprising, determining the level of any of the genes as described hereinabove in a biological sample taken from a tumour, or suspected tumour, wherein tumours expressing elevated levels of DAPK1 and / or reduced levels of NPAS2, NES, CHST7 or EMP1 are predicted as sensitive to treatment with erbB receptor drugs.

According to another aspect of the invention there is provided a method for predicting clinical outcome of treatment with an erbB receptor drug for a mammal, having or suspected of having a tumour, comprising determining the level of any of the genes as described hereinabove in a biological sample taken from the tumour, or suspected tumour, wherein a poor outcome is predicted if:

- a) the expression level of DAPK1 or DAPK2 is reduced; and /or
- b) the expression level of EMP1 or NES is increased.

According to another aspect of the invention there is provided a method for classifying cancer comprising, determining the level of any of the genes as described hereinabove in a biological sample taken from a tumour, or suspected tumour, wherein tumours expressing elevated levels of DAPK1 or DAPK2 and / or reduced levels of EMP1 or NES are predicted as sensitive to treatment with erbB receptor drugs.

According to another aspect of the invention there is provided a method for treating a disease condition in a mammal having, or suspected of having, a tumour, predicted to be resistant or non responsive to erbB receptor drug treatment based on the level of any of the genes as described hereinabove, comprising: providing a resistance-surmounting quantity of an erbB receptor drug and administering the resistance-surmounting quantity of the erbB receptor drug to the mammal.

In a preferred embodiment the mammal is a primate. In a most preferred embodiment the mammal is a human. In a preferred embodiment the patient is a primate. In a most preferred embodiment the patient is a human.

The term "erbB receptor drug" includes drugs acting upon the erbB family of receptor tyrosine kinases, which include EGFR, erbB2 (HER), erbB3 and erbB4 as described in the background to the invention above. In a preferred embodiment the erbB receptor drug is an erbB receptor tyrosine kinase inhibitor. In a preferred embodiment the erbB receptor drug is an EGFR tyrosine kinase inhibitor.

In a more preferred embodiment the EGF receptor tyrosine kinase inhibitor is selected from gefitinib, Erlotinib (OSI-774, CP-358774), PKI-166, EKB-569, HKI-272 (WAY-177820), lapatinib (GW2016, GW-572016), canertinib (CI-1033, PD183805), AEE788, XL647, BMS 5599626 or any of the compounds as disclosed in WO03/082831, WO05/012290, WO05/026157, WO05/026150, WO05/026156, WO05/028470, WO05/028469, WO2004/006846, WO03082831, WO03/082290 or PCT/GB2005/000237.

In another preferred embodiment the erbB receptor drug is an anti-EGFR antibody such as for example one of cetuximab (C225), matuzumab (EMD-72000), panitumumab (ABX-EGF/rHuMAb-EGFr), MR1-1, IMC-11F8 or EGFR11.

We contemplate that erbB receptor drugs may be used as monotherapy or in combination with other drugs of the same or different classes. In an especially preferred embodiment the EGF receptor tyrosine kinase inhibitor is gefitinib.

In a preferred embodiment the present invention is particularly suitable for use in predicting the response to the erbB receptor drug as described hereinbefore in those patients or patient population with a tumour which is dependent alone, or in part, on an erbB tyrosine kinase receptor. Such tumours include, for example, non-solid tumours such as leukaemia, multiple myeloma or lymphoma, and also solid tumours, for example bile duct, bone, bladder, brain/CNS, glioblastoma, breast, colorectal, cervical, endometrial, gastric, head and neck, hepatic, lung, muscle, neuronal, oesophageal, ovarian, pancreatic, pleural/peritoneal membranes, prostate, renal, skin, testicular, thyroid, uterine and vulval tumours.

In a preferred embodiment the present invention is particularly suitable for identifying a patient with head, neck, pancreatic, glioblastoma, colorectal or breast tumour for drug treatment. In an especially preferred embodiment the present invention also is particularly suitable for identifying those patients with NSCLC, more particularly advanced NSCLC including advanced adenocarcinoma that will respond to treatment with an erbB receptor drug as hereinbefore defined.

The present invention provides advantage in the treatment of tumours such as NSCLC, especially advanced NSCLC by identifying "individual cancer profiles" of NSCLC and so determining which tumours would respond to erbB receptor drug such as gefitinib.

The present invention is particularly useful in the treatment of patients with advanced NSCLC who have failed previous chemotherapy, such as platinum-based chemotherapy. The present invention is also particularly useful in the treatment of patients with locally advanced

(stage IIIB) or metastasized (stage IV) NSCLC who have received previous chemotherapy, such as platinum-based chemotherapy. The present invention is also useful in adjuvant therapy or as a first-line therapy.

In a preferred embodiment there is provided a method of selecting a human, having or suspected of having a tumour, for treatment with gefitinib which comprises testing a biological sample, from the mammal for expression of NPAS2, NES, CHST7, DAPK1 and EMP1, whereby to predict an increased likelihood of response to gefitinib.

In a preferred embodiment there is provided a method of selecting a human, having or suspected of having a tumour, for treatment with gefitinib which comprises testing a biological sample, from the mammal for expression of DAPK1, DAPK2, NES and EMP1 whereby to predict an increased likelihood of response to gefitinib.

According to another aspect of the invention there is provided a method of predicting the responsiveness of a patient or patient population with cancer, for example lung cancer, to treatment with chemotherapeutic agents, especially erbB receptor drugs, comprising comparing the differential expression of any of the genes described herein.

In one embodiment the assessment of expression is performed by gene expression profiling using oligonucleotide-based arrays or cDNA-based arrays of any type, particularly where large numbers of genes are analysed simultaneously. In an alternative embodiment, RT-PCR (reverse transcription- Polymerase Chain Reaction), real-time PCR, *in-situ* hybridisation, Northern blotting, Serial analysis of gene expression (SAGE) for example as described by Velculescu et al Science 270 (5235): 484-487, or differential display or any other method of measuring gene expression at the RNA level could be used. Details of these and other general molecular biology techniques can be found in Current Protocols in Molecular Biology Volumes1-3, edited by F M Asubel, R Brent and R E Kingston; published by John Wiley, 1998 and Sambrook, J. and Russell, D.W., Molecular Cloning: A Laboratory Manual, the third edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 2001.

In another embodiment the assessment of expression is performed by measurement of protein levels encoded by the aforementioned genes. For example, an immunohistochemistry-based assay or application of an alternative proteomics methodology.

In another embodiment the assessment of expression is performed by measurement of activity of the proteins encoded by the aforementioned genes, for example in a bioassay.

In a preferred embodiment the biological sample would have been obtained using a

minimally invasive technique to obtain a small sample of tumour, or suspected tumour, from which to determine gene expression profile. Such techniques include, for example tumour biopsy, such as transbronchial biopsy. The profile of gene expression of transbronchial biopsy specimens whose size is about 1 mm may be measured for example using a suitable amplification procedure.

Another aspect of the invention provides a kit for use in a method of predicting the responsiveness of a patient or patient population with a tumour, to treatment with chemotherapeutic agents, especially erbB receptor drugs, comprising a means for measuring the levels of any of the genes as described hereinabove. Preferably the genes are attached to a support material or membrane such as nitrocellulose, or nylon or a plastic film or slide.

In a further preferred embodiment the present invention includes administration of an erbB receptor drug to a mammal selected according the methods described hereinabove.

According to another aspect of the invention there is provided a method of using the results of the methods described above in determining an appropriate dosage of an erbB receptor drug.

In a preferred embodiment the biological sample comprises either a single sample which may be tested for expression of any of the genes as described hereinabove, or multiple samples which may be tested for expression of one or more of the genes as described hereinabove.

The invention is illustrated by the following non-limiting examples in which:

Fig 1 illustrates a xenograft (A549 cell line) which when grown as a xenograft in athymic mice is sensitive to gefitinib. This involved oral dosing, once daily, at the dose indicated. Y axis = mean tumour volume in cm^3 ; x axis = days after treatment.

Fig 2 illustrates a xenograft (MKN45 cell line) which when grown as a xenograft in athymic mice is resistant to gefitinib. This involved oral dosing, once daily, at the dose indicated. Y axis = mean tumour volume in cm^3 ; x axis = days after treatment.

Figures 3, 4, 5 and 6 show examples of specific gene expression profiled across a wider panel of gefitinib sensitive and resistant lines, where definition of sensitivity is based on response to gefitinib when grown as a xenograft, to increase confidence that the expression profile of each gene is truly predictive. Iressa sensitivity is based on xenografts data. The cell lines and the tumours from which they are derived are as follows; KB – head and neck, HT29 – colon, BT474 – breast, DU145 – prostate, LoVo – colon, MCF7 – breast, GEO – colon, A549 – lung,

A431 - epidermoid, H322 - lung, HX147 - lung, RT112 - bladder, MiaPaCa2 - pancreas, MKN45 - gastric, MDAMB231 - breast, PC3 - prostate, Calu6 - lung, SW620 - colon.

The legend key is S=sensitive, U=unknown and R=resistant.

Fig 3 shows EMP1 basal expression in Cell Culture - wider cell panel (Taqman RT-PCR).

Fig 4 shows DAPK1 basal expression in Cell Culture - wider cell panel (Taqman RT-PCR).

Fig 5 shows DAPK2 basal expression in Cell Culture - wider cell panel (Taqman RT-PCR).

Fig 6 shows NES basal expression in Cell Culture - wider cell panel (Taqman RT-PCR).

Example 1**Gene Expression in Gefitinib Resistant or Sensitive Tumour Cell Lines – Cell Culture and Xenograft Studies**

We identified genes useful to predict response to erbB receptor drugs in the clinic. This is based on studies with gefitinib, but the findings are applicable to erbB receptor drugs in general.

The gene lists have been assembled by comparing tumour cell lines which have been demonstrated to be either sensitive to gefitinib or resistant to gefitinib. This definition is based on the response observed when the tumour cell line is implanted into nude mice and grown as a xenograft. This definition has been used for all the pre-clinical studies described herein.

Initially a small panel of six human tumour cell lines were assembled, three which are sensitive to gefitinib and three which are resistant to gefitinib in the xenograft setting defined above.

The sensitive cell lines were;

1. Lovo (ATCC¹ No. CCL-229) – colon tumour cell line
2. KB (ATCC No. CCL-17) – initially reported as a nasopharyngeal cell line (although more recently reported as HeLa derived (cervical carcinoma))
3. HT29 (ATCC No. HTB-38) – colon tumour cell line

The resistant cell lines were;

1. MKN 45 (source - Nottingham University, UK) – gastric tumour cell line
2. Calu 6 (ATCC No. HTB-56) – lung tumour cell line
3. PC3 (ATCC No. CRL-1435) – prostate tumour cell line

¹ATCC = American Type Culture Collection

The cell lines were grown both in cell culture and as xenografts, RNA prepared and the basal expression profiles determined by measuring RNA expression on the Affymetrix microarray platform. As part of our studies, the term 'basal' has been used to indicate constitutive or steady state expression levels (rather than expression levels which are modulated as a consequence of administration of an erbB ligand or gefitinib to the cells). Figure 1 illustrates the sensitivity of A549 xenografts (used in Example 3 below) to treatment with gefitinib. Figure 2 illustrates the resistance of MKN45 xenografts to gefitinib. See Example 2 below for analysis of results.

Example 2

Statistical analyses of cell culture and xenograft data sets

The following statistical analyses were performed separately for cell culture and xenograft data sets. Probe sets were eliminated if their signal was not distinguishable from background noise across all RNA samples in the set. Mixed ANOVA (see for example Scheffe, 1959) was applied separately to each remaining probe set to generate p values. The p values were then used to calculate Q values (Storey). The Q values indicate the expected proportion of genes in a gene list which are not truly differentially expressed but have been falsely discovered (False Discovery Rate or FDR). Q value cut-offs appropriate in the different studies were identified and applied, based on graphical examination of the p value and Q value results, in conjunction with fold change. The final genelists for each study were generated using Q value and fold change (FC) cut-offs. The different genelists were then combined to display an overall list of genes which showed consistent differences in expression profiles between the cell lines in the sensitive and resistant groups.

Further details of the analysis procedures are provided as follows. Fold change (FC) was calculated based on the mean of sensitive cells divided by the mean of resistant cells. To generate gene lists, FC cut-off of two-fold (2X) change in either direction was used in all cases. Furthermore FDR Q values were used to narrow down the lists and obtain the most significant gene changes across sensitive versus resistant cell lines. In the case of cell culture, Q value cut-off is 0.3. In the case of xenograft, Q value cut-off is 0.6. The different cut-offs used reflect the different design and variance values associated with each experiment.

In cell culture studies, lists were obtained based on the above criteria for cells grown either in full serum containing medium or in charcoal stripped serum. In the xenograft study, the same as above was performed for separate sets of tumours harvested at 18hr intervals. Gene lists contain some redundancy in genes where appropriate to illustrate consistency of results obtained for example with different probe sets.

Example 3

Identification of predictive genes

Genes which have not previously been identified as predictive of erbB receptor drug sensitivity are listed in Table 1. Other genes which we have identified to be optionally used in combination with Table 1 genes are listed in Table 2.

Key to Tables:

'Affymetrix ID' – the Affymetrix probe set identifier

'Sequence' – target sequence relating to the Affymetrix probe set indicated by 'Affymetrix ID'

"+" if up in sensitive" means that the gene is relatively highly expressed in sensitive cells. (Consequently, absence of a "+" means that the gene is relatively highly expressed in resistant cells).

'Gene Title'- The current annotation of the gene relating to 'Affymetrix ID' based on UniGene 133

'Gene Symbol' – shorthand synonym for the gene title

'Locus Link' & RefSeq Transcript ID' are provided for gene identification purposes.

Combining genes has the potential to generate an improved diagnostic over genes used in isolation. Collective gene expression profiles (at the RNA and/ or protein level) may be more likely to identify patients most likely to benefit from gefitinib rather than the expression level of one gene in isolation.

It may be more practical when developing a pre-treatment response prediction diagnostic to work with a truncated gene list from tables 1 and / or 2. A number of criteria have been used to shorten the gene list to identify those genes which are most predictive of response. Firstly the statistical (p values and Q values or FDR values) can indicate the statistical significance of a gene.

Secondly, the differential expression (fold change) between the sensitive and resistant groups indicates the potential sensitivity of a marker to be used in a diagnostic test (highest fold change between sensitive group and resistant group is preferred).

Thirdly, we have performed RT-PCR based expression profiling across a wider panel of gefitinib sensitive and resistant human tumour cell lines to increase confidence that the expression profile of each gene is truly predictive. Figs 3, 4, 5 and 6 show examples of specific gene expression profiled across a wider panel of cell lines as set out below.

The sensitive human tumour cell lines, where definition of sensitivity is based on response to Iressa when grown as a xenograft:

- a. BT474 (ATCC No. HTB-20) – breast tumour cell line
- b. DU145 (ATCC No. HTB-81) – colon tumour cell line

- c. MCF7 (ATCC No. HTB-22, sourced from ICRF (now CR-UK), London), - breast tumour cell line
- d. GEO colon tumour cell line. RNA obtained from Fortunato Ciardiello, Cattedra di Oncologia Medica, Dipartimento Medico-Chirurgico di Internistica Clinica e Sperimentale "F. Magrassi e A. Lanzara, " Seconda Universita degli Studi di Napoli, Via S. Pansini, 5-80131, Naples, Italy.
- e. A549 (ATCC No. CCL-185) – lung tumour cell line
- f. A431 (ATCC No. CRL-155) – epidermoid cell line

The resistant human tumour cell lines, where definition of sensitivity is based on response to Iressa when grown as a xenograft:

- 1) HX147 - (source: ICRF (now CR-UK), London) – lung tumour cell line
- 2) RT112 - bladder tumour cell line (DSMZ No ACC 418)
- 3) MiaPac2 (ECACC 85062806, ref. no. 001611) pancreatic tumour cell line
- 4) MDAMB231 (ATCC No. HTB-26) – breast tumour cell line
- 5) SW620 (ECACC CCL-227) – colon tumour cell line

ATCC = American Type Culture Collection

DSMZ - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (German Collection of Micro-organisms and Cell Cultures)

ECACC = European Collection of Cell Cultures

In isolation, each of these genes is reasonably predictive of gefitinib response, but collectively they can be applied to make predictions with a higher level of confidence.

The Affymetrix probe sets identifiers for the genes in the above diagnostic genelists are indicated in Tables 1 and 2. Current Affy IDs are based on Affy U133 chipset. For the avoidance of doubt, the target sequences of the Affymetrix probe sets which identified the listed genes are also provided in Tables 1 and 2.

Without wishing to be bound by theoretical considerations, it is contemplated that the specific sequences used to detect target genes in the Examples may define specific splice variants or sequences in homologous genes. Therefore in one embodiment, a listed gene for use in the method of the invention is defined by the specific sequence used in said Examples. In another embodiment, a gene for use in the method of the invention is not limited by the specific sequence used in these Examples. Indeed the fact that some genes in Tables 1 and 2 have been identified using different sequences (gene “redundancy”) and confirmatory RT-PCR studies (see

Example 4) provides evidence that usefulness in the method of the invention is not generally limited to the specific sequences used to measure the target gene.

Note, in the event of a discrepancy in the sequence between Tables 1 and 2 and the Sequence Listing, the sequence as provided in the Tables is preferred.

Table 1: as described in priority application US60/619027 filed on 18/10/2004.

Gene Symbol	Gene Title	AffyMatrix ID	+ up in sensitive	Sequence	LocusLink	RefSeq Transcript ID	SEQ ID NO.
ACOX2	"acyl-Coenzyme A oxidase 2, branched chain / acyl-Coenzyme A oxidase 2, branched chain"	205364_at		Gtgcagcatitacagaacctgacgcacatccggagctgaccagcaacgaggttgga accagcatctctacacctccaggctgctaaggfgcactgctactatgtcacgtg aagggtttacagaagaagcttggagaaactgaaaaatgaaccca-ggattcagcaggt gctcaagcgccctctgtgacctcatgccatcacatgaatcttgacaaacgttgact ttctcatgacgcctctctgtctgtgcccaggtggacatggcaagaacagctaccctg gacctgctccgctgatcccggaagatgccatccctgtttaaactgatcttttgactcaacc gatcaggtttaaatcagacctgtgctgtatgatggaaacgtctacgaacgcctgttcc agtgggtcagaagtc	8309	NM_003500	SEQ ID NO:1
ACTR2	ARP2 actin-related protein 2 homolog (yeast)	200729_s_at		gagcttaagcatctggctgttttgtaatgctctgtttatccagaagcalttaaggtaacccat tgcacagatcatcttgcacatattctttatataacigaccagtgcttaataaacaag caggtactacaaataattacttgcgcagtaggtatlaattgggttttaaaaaataacatlg gaatacaggaactgttgccaattggglaattttcaltatgtttgtttgtttgatttgaaac ctggaaatacgaataattgactgtttaaattgttggccaaaaataacagatttaatt tttttattgtactgaaaaactaatcatactgttaattctcagccactcttgaaagctgaaat gaaagactcttggatttttgaacaggtagaacacttctgcacgtgtcagaataactaa ttatgaatcctgtcgggtattcctctgtatctgaaaaaaaataccaaatagtaaccatacalg agttattctaa	10097	NM_005722	SEQ ID NO:2
APOL1	"apolipoprotein L ₁ / apolipoprotein L ₁ "	209546_s_at	+	agaatagagaggaggtctggaaggaaccagcaatgagaaggccaggaagaaagaa agcgtgaaatggagaaagcccaagaggttagaacaagtggtacacaggagaaga aacacgcgctccactacacagaccagccacaggttcaatgtcctcgaagaatgaag tcttctctgtgtatgctccctgacctgtcttcacagatccactctcctctctctgtg gggccatatctcagtcagcagcagcgctctgatgatgtgtgtgtgtgtgtgtgtgtgt atgggtctctccagggttactaaagggtgcatgtccctgtctgaacacatgaagggtcag gtgt	8542	NM_003661 / NM_145343 / NM_145344	SEQ ID NO:3
C10orf10	chromosome 10 open reading frame 10 / chromosome 10 open reading frame 10	209183_s_at		aactcatagctctgtgtggtgcatggagagttcccccattgatgagggtccaaagata gaatctgtacactcagctgtctacatccacccacccacacacacacacacaggggc ctatctgcatgttcagggtccacagctgtatgtgagcagcagggcactgtccagctgtc cactgggaaggtcaagatgtcttaaggccacaggttcagggtcacttggagcttgaagg accctagttctcagggacatctgcacgaagaaggttggggcatcaggggaacgcgga atcaggtctgggactgatcagaggtgaaaggacagagagagagagagagagagagga ttgagctggggggcaacagccacgtccactgggaggtctctgcacactctgcct gttgagctgacgtcagctcgtatctcttttttggcgtatttttaattgcttggatttghaaatg tttctctctctgttaaggtgtgtt	11067	NM_007021	SEQ ID NO:4

CALM1	"calmodulin 1 (phosphorylase kinase, delta)"	211984_at		801	NM_006888	SEQ ID NO:5
CALM1	"calmodulin 1 (phosphorylase kinase, delta)"	211985_s_at		801	NM_006888	SEQ ID NO:6
CD44	CD44 antigen (homing function and Indian blood group system)	210916_s_at		960	NM_000610	SEQ ID NO:7
CD44	CD44 antigen (homing function and Indian blood group system)	212063_at		960	NM_000610	SEQ ID NO:8
CDS2	CDP- diacylglycerol synthase (phosphatidate cytidyltransferase) e) 2	212864_at		8760	NM_003818	SEQ ID NO:9

[illegible]

DPYSL 3	dihydropyrimidina se-like 3 / dihydropyrimidina se-like 3	201431_s _at	tgaggggccacggggtgggtgagtggaaggggtgttgggaattgttaaalccgttac ccgtagtagagctattctgtacttaagttttcagagtggaaggtggaaggtgagtcacot gaaatgggtttacttaaaatccctccctccatcttctcgcagctgtctatctgaggt gtcatgttccacaaagggtgacacctgagcctggatcttccatccctcaggaagc ccttccagtaggtgggtgcaatcccaactctctgccaagctccagggcttcc ccgtgaaaactccagctgagctccagatacaactcatgggtgctccctgggagccag catctattgaaagtccctcttgaacacgtgtgtgggtgttcagctctgtctgtgggt atggacagacgaatctctgtatctgtctgtgtagctgtgaggaagctctggaacgtg a	1809	NM_001387	SEQ ID NO: 15
DUSP4	dual specificity phosphatase 4 / dual specificity phosphatase 4	204015_s _at	ggctccagcaagggtgagcggggccgcatgcccgcagcaaaagtgggacgtgagc agctgggagcagggagaccgagctcctcccatcttctctctgtgccaacgacgag ggcagccagaatggcaataaaggactccgaalacataataaaagcaacaagaaca ctccaactgagcaataaacggctgcccgcagcagccagggagagacctgtgtgtt atgtgtcagtttcttctccgatagaattcttctacatcttctttaaagagctga agtgatgaacccacacagatctcgaatgtgccaacacagcttacttaaaagggg aggaaaggaggccaaagggtgagaagacaagtctccagaaggtgctgtgtctg gatacgtggggcccatggaagagggtggccgagcagctgggctgtctactgg cgagaaggagaagctgcccgggagagcagagcggtgcaaggccaacgcaagaac aagacagggaagtgtgtccgcgagcctgcccagcggggccaacgcccgcg ggagtcctcagcccaacccgcagagcagcagcagcagcagcagcagcagcagc caactgtcagagagcagcagcgtgagacagcagcgtgagcagcagcagcagcagc ctccatcccgatctctgtgttaaggcaagcagcagcagcagcagcagcagcagc gctctcatcagcttccacccgcgcgaggtgtgtgtgtgtgtgtgtgtgtgtgtgt gtttgt aagccagctgcccagctgt a	1846	NM_001394 / NM_057158	SEQ ID NO: 16
EIF3S4	"eukaryotic translation initiation factor 3, subunit 4 delta, 44kDa / eukaryotic translation initiation factor 3, subunit 4 delta, 44kDa"	208887_at	gatacgtggggcccatggaagagggtggccgagcagcgtgggctgtctactgg cgagaaggagaagctgcccgggagagcagagcggtgcaaggccaacgcaagaac aagacagggaagtgtgtccgcgagcctgcccagcggggccaacgcccgcg ggagtcctcagcccaacccgcagagcagcagcagcagcagcagcagcagcagc caactgtcagagagcagcagcgtgagacagcagcgtgagcagcagcagcagcagc ctccatcccgatctctgtgttaaggcaagcagcagcagcagcagcagcagcagc gctctcatcagcttccacccgcgcgaggtgtgtgtgtgtgtgtgtgtgtgtgtgt gtttgt aagccagctgcccagctgt a	8666	NM_003755	SEQ ID NO: 17
EIF5A	eukaryotic translation initiation factor 5A	213757_at	atgt ctccagatgctcagagagggggcaggttccctccctccctctctctctctccat ctaaagggt gggt agtggt ctgt atctgt gagggcagaggggggaggggaggggaggggaggggaggggaggggaggggagggg gggt gggt ctgt gaggggaggggaggggaggggaggggaggggaggggaggggaggggaggggagggg gaggggaggggaggggaggggaggggaggggaggggaggggaggggaggggagggg ccccagctgt aatggcagtgccccccagcagcagcagcagcagcagcagcagcagcagcagcagcagc cccatagggagctgt	1984	NM_001970	SEQ ID NO: 18
FADS2	fatty acid desaturase 2 / fatty acid desaturase 2	202218_s _at	ctgt atctgt gagggcagaggggggaggggaggggaggggaggggaggggaggggaggggagggg gggt gggt ctgt gaggggaggggaggggaggggaggggaggggaggggaggggaggggaggggagggg gaggggaggggaggggaggggaggggaggggaggggaggggaggggaggggagggg ccccagctgt aatggcagtgccccccagcagcagcagcagcagcagcagcagcagcagcagcagcagc cccatagggagctgt	9415	NM_004265	SEQ ID NO: 19

[illegible]

GSPT2	G1 to S phase transition 2	205541_s_at	aagcaattttcgtgatgcctcgcgaagatactcgtgaggagaallgacagcaaaagtcca ccactctcttaattacgtcccatgattgactttctcataitttgcagaagaaatttca cagcaaaaattcattgtttgcagcttccatgttgatctgttgcactgatgaattta ccctcaagttctctcgtgaccactcgtctcgtggacaattcaglaaagcttgta agtgatggcagcaattgcctacgaaagaaataaalgactttaattttcattttctt ttaggataattagaccacccctgttccagcacaacacagagtgacaggtgtgtg caggatcggagcagcccgagctccaaaggtgggtgtttgtttttaaaggaga gaggaggggtgagtgcaagggaaggagggggcgaggtcctgcggcggc agggaagcctcgtccctcactcctccaaaagagacccctcctglaaggaagc aggctcccgagggtttcttccatgtgtttctcctcgtgttaaaggaactttttaaa aaacagacccgttttagattatagcattgactttacacacatcacacagaaaaa aatccttcaaaattcattcctcctcctccttttccaagggaagaaatgggcaaaag tggcctggcctcgtgtggtggtcgtggtcggagagagaagaaatgggaaaga cattcactggtgttctctttttttgtgccccccgcccccatccataatctgla ac	NM_018094	23708	SEQ ID NO:24
H2AFY2	"H2A histone family, member Y2"	218445_at	gaggaattgctcatgtggcacaacalgggtgcaacggtgatttccatctcgtgaaa gttaacctttatttctgtatgtgtacaatcaaacacactcctcctcctcctcctc atacctcttttctacatgaaaataaaagctgtggccaatggaacagtaagaacat cataaattttatataatgattattttgtgggaataattttaggactgttctgtgtg tgtgtgcagcagctaaataagcagacatgacatttaccatttccatttgcgaattgga tgtttgcagagaaagatacaagacgtttaactgcaggtgacttctcctgtcctgtg agtgctcctaacttatttctttatgtagaattgctgtatgattgactttgaatcgt tgactgtgaaaattctcctagtgattatcactgctgtctgcaacaataaataaca gcctcgtgaltccc	NM_018649	55506	SEQ ID NO:25
HMGGA2	high mobility group AT-hook 2 / high mobility group AT-hook 2 / high mobility group AT-hook 2	208025_s_at	gaggaattgctcatgtggcacaacalgggtgcaacggtgatttccatctcgtgaaa gttaacctttatttctgtatgtgtacaatcaaacacactcctcctcctcctcctc atacctcttttctacatgaaaataaaagctgtggccaatggaacagtaagaacat cataaattttatataatgattattttgtgggaataattttaggactgttctgtgtg tgtgtgcagcagctaaataagcagacatgacatttaccatttccatttgcgaattgga tgtttgcagagaaagatacaagacgtttaactgcaggtgacttctcctgtcctgtg agtgctcctaacttatttctttatgtagaattgctgtatgattgactttgaatcgt tgactgtgaaaattctcctagtgattatcactgctgtctgcaacaataaataaca gcctcgtgaltccc	NM_003483	8091	SEQ ID NO:26
IER2	immediate early response 2 / immediate early response 2	202081_at	gaggaattgctcatgtggcacaacalgggtgcaacggtgatttccatctcgtgaaa gttaacctttatttctgtatgtgtacaatcaaacacactcctcctcctcctcctc atacctcttttctacatgaaaataaaagctgtggccaatggaacagtaagaacat cataaattttatataatgattattttgtgggaataattttaggactgttctgtgtg tgtgtgcagcagctaaataagcagacatgacatttaccatttccatttgcgaattgga tgtttgcagagaaagatacaagacgtttaactgcaggtgacttctcctgtcctgtg agtgctcctaacttatttctttatgtagaattgctgtatgattgactttgaatcgt tgactgtgaaaattctcctagtgattatcactgctgtctgcaacaataaataaca gcctcgtgaltccc	NM_004907	9592	SEQ ID NO:27
KIAA0121	Vestigial-like 4	214004_s_at	ccactcgtgaccccgtgtggaaggagatttcccgaggagcctgggcaagaattac aaggagcccgaggccggcaaccacactcgtgtccatcaogggctcccgtagacacc acttgcacaaagcttgggtgacacgtgcttcagatcaaaaggcccaaggacgga gtaaccaagccctgagtcgcgtcctcgtcgaaggccacgcccccctcctgc ccacatggtcaagccacagtcacitccccctcctgtgttccctgaagggaagccctc caacaacacgtggatctgcagtggttgcctgagcttgaacagtca	NM_014667	9686	SEQ ID NO:28

KIAA0931	KIAA0931 protein	213407_at	+	attagctccaaagccattcagtgatgcttcagcaacacataggaactgtctagtgctcacttttactctctctgggggagggcttcgactcccaatcatgaaggcaagttaactcttccagtgtagtgaactttggccacalagttggggaanacactctdagatggaaaaagcagctacagtcactctgtctgttgcctcaattggtgatcagtcagtcacacataagctctgtattctaaattcatgcactctccagatgcgtataggggtttctctcactgttgccaaatggatgtccatccagacgtgggctcatatctactcaggttttggc	23035	---	SEQ ID NO:29
KLHL7	kelch-like 7 (Drosophila)	220239_at		agttgatacagagccctccagagtggttatgctttcactctgtgatgatccttagtggcaatgaatgaacgtccagatgtttgtgcagtgagccacactatctgcaggatacgtccaaagcccccagtgaaatgcctgaacatgcagatagctgaatcatatatactgtgttttatgatcatcatcagctgcctatgctgaagt	55975	NM_018946	SEQ ID NO:30
LAMC2	"laminin, gamma 2 / laminin, gamma 2"	202267_at		aagaaatgttctactcacactcagctggtccacatccatccctccattcatctctccalocatcttccalaccibccalocalcttccacaatatattattgagtaacctagtgtgccaggggctggggacagtggtgacatagctctgccctccalagagtgattgctatgtgagggagacagcaatttttaaaaaataaattaaacttacaacattgtttgtcacaaagtggttattgcaataaccgtgtgttgcaacctctgtctcaacagaacatatgttgcaagaccctccalgggggaactgtgatttggcaaggctgacagagctctgggttggcaattttctgcatccacgtgctactctgtgcccttctacaactgattgcaacagactgttgagttatgataacacagtggtggaattgctggaggaaacacagaggaactccactggctgggaagactatggctgctctggc	3918	NM_005562 / NM_018891	SEQ ID NO:31
MLL3	"myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 3 myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 3"	204918_s_at	+	aaggcattccacaggaatcatcatttaaaaaaagaatctgtgctgttttctaaaaaataaaacactgtgtgaaatcttaattggatctattatgtagcagagtttcagctcttcacgctgttactcttctatccaaaaatctcggaaatctcggaaatcttcttgatattgttcttagacattttatgaaataataaactcttctggggaataatcttgattctgccataacagatattgattaaactgtagattacagtggtgttcaataactgtttagtctgtctaaatattccagaggaattctgtgattgtggaagacgtgtgggagtggggattttttgtctgtgtaacccgtgttgaaacttgaaactgaaatctgtcctgtggcatgcaaaagaaaagcaaatatttttaaaagaaaaaaccaagactttgtgtgctatttccatcttccat	4300	NM_004529	SEQ ID NO:32
MNAT1	menage a trois 1 (CAK assembly factor) / menage a trois 1 (CAK assembly factor)	203565_s_at		ccagccactgcagatagagacatatggaccacatgttctgagcttgagatgctaggaagctgggtatttaaacatgtcagagctgcctcaccacagacactgctggaggtctactctctctgtgtgcacagaacacacaggaatgattcagtggtgttcttctggcaggtgaacacattataaagatttggaactggagctgaaccagggagctagcaaaagtaaacgacactataaaattatagctatgtgcagctgcaacaacacagctctccactacgaactgtgttaa	4331	NM_002431	SEQ ID NO:33

[illegible]

PCDH GC3	"protocadherin gamma subfamily C, 3"	209079_x _at		cagaaggtctcagccacagagtgagggtcttcaacaggggccctcgcctctcgaagc ctcagctcttcaacttgcaggtgcccgttcttctcctggaagggccactgcacaggtccc cagtgccgcccctagtgccatagctgtttaaaggtccacagtgccctcttgcata gactctctccacacccctctgccttgggtccacggccatccagcgggtgcga gagaacccacagactgccttcaagtagtgcagcccccctcctcttctggtggt agaatagcagtagtgcaggtggttcttcaagtagtgcaggtggtgcagcgggc ggcgggtccgcgcagccgtctgctctgactgcagccgcggccgtggtggttgg tgcgtgcacgcgcgaagggcgaacccctcccccgtactgactctctataagcgtt ctctgcagtagtcacgtgctccacacccctctctgctgctcagcgaaggttta ggatgggtctctcaacagggccctcgcctctcgaagcctcagctctcacttgc aggtgccttctctcctggaagggccactgcacaggtccacgtgcgcccctagtg gccatagcctgtttaaaggtccacaggtgcctcttgcatagacctctctccacccc ctctgccttgggtccacggccatccagcgggtgcagagacccctctccacccc ccctacagtagtgcagcccccctctcttctggtggtggaatagccagtagtgc agtgcgtggttcttcaagtagtgcaggggtgcagcgggcggcgggtccgcga gcccgtctgctgactgcagccgggtgcagccgtggtggttgcgtgctgcagcgc aaggcgaacccctcccccgtactgactctctataagcgtctctctcgaagtagcag tagctccacaccccccctctctctgctcagcgaaggtttactctataattatggc ttttctctgcacaa	5098	NM_002588 / NM_032402 / NM_032403	SEQ ID NO:38
PCDH GC3	"protocadherin gamma subfamily C, 3 / protocadherin gamma subfamily C, 3"	211066_x _at		gcaagcttgggtcagctaacaggacacatgattaaactggcatttcaagctcaag gaagctcgaagcaggttaggacacaggtcccttgcaggtgcagaggggtcctgt gggtgctgggtactccagaggtgcacgtgggaaggtcagcggagcccagtgcc ctctgtgcatagacctctctccacacccctcttgccttgggtccacccctccag cggggtgcagagacacccagacctgccttcaagtagtgcaggtgcttcttcaag tttgcgtggtggaatagccagtagtgcaggtgcttcttcaagtagtgcaggtg gggcagcggggggcgggtcgcgcagccgtctgcttgcagtagtgcagcgggc cgt tctataagcgtctctctcgaatagtagcagcagcccccctcccccgtactgctc acgcaaggttta	5098	NM_002588 / NM_032402 / NM_032403	SEQ ID NO:39
PCDH GC3	"protocadherin gamma subfamily C, 3 / protocadherin gamma subfamily C, 3"	215836_s _at		tgacgcccctgaagatgacctggcagctgcactgcttacctgtctgctgcagac gcccactcggacacagggcctctacatggagggagggcgtgcccattgcgagcag actatgagaagatgttggcagcgaatgacctggcgtgactcaagatcagcgtgg ggacccctctggagggcctgggtcagctgcgtgcagctgacacccctctctgtgcga tatgcaatcaacccctggaaggaagacctctcctccacgaagaggaagacctct gaaagacacagctctctctcaggtgagccccttgcacacagctgcgcgtgg cccctagcctgagggggtcggagtcggtggccctgcaattctgggtgaggggtggaat	5098	NM_002588 / NM_032402 / NM_032403	SEQ ID NO:40
PDJIM 7	PDZ and LIM domain 7 (enigma) / PDZ and LIM domain 7 (enigma)	203370_s _at		tgacgcccctgaagatgacctggcagctgcactgcttacctgtctgctgcagac gcccactcggacacagggcctctacatggagggagggcgtgcccattgcgagcag actatgagaagatgttggcagcgaatgacctggcgtgactcaagatcagcgtgg ggacccctctggagggcctgggtcagctgcgtgcagctgacacccctctctgtgcga tatgcaatcaacccctggaaggaagacctctcctccacgaagaggaagacctct gaaagacacagctctctctcaggtgagccccttgcacacagctgcgcgtgg cccctagcctgagggggtcggagtcggtggccctgcaattctgggtgaggggtggaat	9260	NM_005451 / NM_203352 / NM_203353 / NM_213636	SEQ ID NO:41

[illegible]

<p>serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9 / serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9"</p>	<p>209723_at</p>	<p>+</p>	<p>ttccaccatcgtgcgtgtgtgacatccctggcccaaggaacatccgcctaccacag cctcccaaaagtcagagattacagggcataagccacatgagccacgcttcagta tctttatgtaaatataaacaatcgaacattatgatacatatgcagatactatgcatctt tttatagtggaagtgctatgattatgtctgactgaattcctcatctatgaattgca ttacacacactcttctgctgttttaccatgctgttgcctttaaagaatattatccctt gtttattattctctcattctctgattgcttttaa</p>	<p>5272</p>	<p>NM_004155</p>	<p>SEQ ID NO: 46</p>
<p>sine oculis homeobox homolog 1 (Drosophila) / sine oculis homeobox homolog 1 (Drosophila)</p>	<p>205817_at</p>		<p>ccggaggcaagaagacggccggcggaaggccaaggaagggaaggaacacccga aacaataactctctcccaacagcagaacaactctctctctggaagggggca agccctatgctccagctcgaagagggaattctcaccccaaaagtcacagaccag aactcgctctctgctgcagggcaatattggcgacggccagagatcacaactatctc tccgggtttaacagctcgcagccagcagctgcagccgctgcagaccaccagatcag ctccaaactctctcgcggccctccactccagctggtggactggggtcctaaagt ggggaggagctggggtcgaaggatctcggagcagcaaccaactgcagcgact agggacactgtaaatagaaatcaggaacttttgcagctgtttctggaggtgttgcg cataaaggaaatgggagactttcaacaatatcttttaaaaaatcaaaaaccaacagcat ctcaagcttaa</p>	<p>6495</p>	<p>NM_005982</p>	<p>SEQ ID NO: 47</p>
<p>"solute carrier organic anion transporter family, member 3A1 / solute carrier organic anion transporter family, member 3A1"</p>	<p>219229_at</p>		<p>ggctgacacacagtgactttgtctctactctgacccctagacaactctggggaggga cctgtgcgcgaacacagacacataggaacaaagtattatataaactgggaagacc atgagtgtgtgaaacacatgagctcgtttttagtgactaaaggagggtggaactct gttatgtaactcaagggtcatttttcttaaaaaaagaaaaaaggttccaaaaaaa accaaaactcagttacacacagcagacagatgcacacacacagacagacagac aacccgacttgccttttctcagcagcagccagacagagattccagaataagagga gaatgacatcgtgcgcagggtctcggagggccactcgcgcgtggggccacagag tctacttgagggcacactcagtttctcaggtgctgacagctgcaagcaacaggcact gccaaaatccagggaacagtggtggccagcttgaggatggagc</p>	<p>28232</p>	<p>NM_013272</p>	<p>SEQ ID NO: 48</p>
<p>"serine protease inhibitor, Kazal type 1 / serine protease inhibitor, Kazal type 1"</p>	<p>206239_s_at</p>	<p>+</p>	<p>gagacgtgglaagtcgcgtgacgtttcaactgaactcggacgcagaactcagcca tgaagtaacagcgcacttctctcagtgcttggccctgtgagctatctcgtgaacact ggagctgacctccctgggaagagagggccaaaatggttaacatgaactaatgagtgac caagatatacgacctgtctgtgggactgaggaataactatcccaatgaatgcgtgtt atgtttgaagtcgggaacacgcagactctatctatcattcaaaaaatctgggaccttg ggaacacaggttttcaaatccacatcaatccacgc</p>	<p>6690</p>	<p>NM_003122</p>	<p>SEQ ID NO: 49</p>

[illegible]

[illegible]

Table 2: as described in priority application US60/619027 filed on 18/10/2004.

Gene Symbol	Gene Title	Affymetrix ID	+ up in sensitive	Sequence	Locus Link	RefSeq Transcript ID	SEQ ID NO.
AGXT2L1	alanine-glyoxylate aminotransferase 2-like 1 / alanine-glyoxylate aminotransferase 2-like 1	221008_s_at	+	gctgaagaagccacacatagaacgctagggagcagcaccacgactcccaaa gaaaatccacgacgaagaagaagaatggaatgacgagcagcagcaccacgct cagtaagagcctcaagacacagcagctgattgcatatttaagaagaagcagctgctc agagttacagagaatgagtagatgctcctcagcgtcttaataagcctctatataccct aaagggtgaatgctgagttagattcaataaagaagaagaagtaaatgagtaacaga ataaaccacagtgataatcaaacatgcaagattattgctcagactagcctggt aatcttcagtgattcgaagcactgattatttatttaaatgtaagcctgcaaa ctcaaataaatggcagattacctctcatgttttaattgtgcaaatagagagca aagtataacaggtgctcctcactttgagact	64850	NM_031279	SEQ ID NO:58
AKAP12	A kinase (PRKA) anchor protein (gravin) 12 / A kinase (PRKA) anchor protein (gravin) 12	210517_s_at		gtgccatagtcaggcgtgggagccttaagcctcagttatataaaccacgaaaa acaagcctcctagatgaacattcctgatcaagggtacaattcttaaaattcacta atgattgaggccatatttagtgactctgaaatggcacttcttattacacgga gtgctcaaacctaaagaacatttgaacatacagaatgtctattgctattggga aatcttcttaaacccagtgagggttagaagaagttatattctgtagcaaatga actttacactctttctactctgtatgtgtgttgaccgaataaggtgcttaactga ggcaagtaggaatagttttatattgtaagaaagaagaatgtgtaagtttga ttctactctatagctggactgcattccacacatgcaatgaaataagtcaggtctta caaatggtatttgatagactggaattgtgttgccattgtgccaattgtgccaatt gggatgctattgtgccattgtcaaatgtcaagaacagacgctctcttcttggcgg acaacacttacaatccatgaagggtgctggcacaagatgaagaactctgacc aggatcatggtatcccgagtgagattgacctgctcaacatccggagggaattc atgagaataatgaacagctctccacaaagccattgagggtgacacctccgga gactctgaaggcctgctgctctctggtggtgagactagggccacacgctt tgccggcactctgccagaagaatggtatcagcaccacgacgccaatggccaag cctgattgtccagctccagacacgaagggcagggggggtggggggggg gttgggtgggctctatctatctatgagccttaggaacgctccacccacgggc catcgaggggccagcagcgctgagcgggtgaataaacgtagccatagatcctgt cc	9590	NM_005100 / NM_144497	SEQ ID NO:59
ANXA6	annexin A6 / annexin A6	200982_s_at		atttcaaaattctgactcagcagagaatgcaaatatataagacaccttgaagca gtacatgcaaatgcaagcaagaatattcgtgaacggtggtgggaaggtcc atgaacacacacagatgattgacagtgattatcaaaaattgcattagcgcca tagctgctttatgtctgtgactcacaagctgtgctgtatttaccagcttia gaagcaatactgcaggaaatagaaaggaagcgtgaggaacgaaagaaa cttcgacaaagaaatggaaatgtacatgctatagcatalaacgaagataaata caggatatacactggagcactgccaaagctatagccataaatgatgagctgct ctcttcacagtggatcaataagacaatggacccttttgtatgattgttttaacttca attgctacattttatgctatttctgata	309	NM_001155 / NM_004033	SEQ ID NO:60
AREG	amphiregulin (schwannoma-derived growth factor) / amphiregulin (schwannoma-derived growth factor)	205239_at	+	atttcaaaattctgactcagcagagaatgcaaatatataagacaccttgaagca gtacatgcaaatgcaagcaagaatattcgtgaacggtggtgggaaggtcc atgaacacacacagatgattgacagtgattatcaaaaattgcattagcgcca tagctgctttatgtctgtgactcacaagctgtgctgtatttaccagcttia gaagcaatactgcaggaaatagaaaggaagcgtgaggaacgaaagaaa cttcgacaaagaaatggaaatgtacatgctatagcatalaacgaagataaata caggatatacactggagcactgccaaagctatagccataaatgatgagctgct ctcttcacagtggatcaataagacaatggacccttttgtatgattgttttaacttca attgctacattttatgctatttctgata	374	NM_001657	SEQ ID NO:61

[illegible]

[illegible]

Gene	Protein	Position	Sequence	SEQ ID
CDKN2A	"cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)"	209644_x_at	+	NM_000077 / NM_058195 / NM_058197
CEACAM7	carcinoembryonic antigen-related cell adhesion molecule 7	206199_at	+	NM_008890
CHORDC1	"cysteine and histidine-rich domain (CHORD)-containing, zinc binding protein 1" / "cysteine and histidine-rich domain (CHORD)-containing, zinc binding protein 1"	218566_s_at		NM_012124
CLU	"clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)"	208791_at	+	NM_001831 / NM_203339

[illegible]

[illegible]

EMP1	epithelial membrane protein 1	213895_at		2012	NM_001423	SEQ ID NO:85
EREG	epiregulin / epiregulin	205767_at	+	2069	NM_001432	SEQ ID NO:86
FGF2	fibroblast growth factor 2 (basic)	204421_s_at	+	2247	NM_002006	SEQ ID NO:87
FGF2	fibroblast growth factor 2 (basic) / fibroblast growth factor 2 (basic)	204422_s_at	+	2247	NM_002006	SEQ ID NO:88

FLJ22662	hypothetical protein FLJ22662	218454_at	+	gtagctatccaciggttagtcagaaagctgggcttggactacitcattgatttagctcc acgagccaaatttccggcgagccaaagggaagtgactgatacggcattcca tgaattatataatcgcgatacaacaattataaagagatccitacagtagagtgga cccttgaataccatctgctgcctgagagcctgaactacacctaaccocaaagct ggagtggtatgacacaaaggcgagatatactacatgaatcagtaacacat cctatgcctaagtggtccacagtaacaggctccctgcttcttctggggac cgttcaacaaacatcatalcagggcagtgccagaggtctcaacacttgatttatt accatgaaacccaatttgaacactgataataaaggaaggaggagatgacgga clagaagactgtaataagatacaaaaggacattattttagctatttttcccatca gaat	79887	NM_024829	SEQ ID NO:89
GADD45 B	"growth arrest and DNA- damage-inducible, beta / growth arrest and DNA- damage-inducible, beta"	207574_s_at		cccatcagagggctccagactgtccaclogggggtggagtgagactgacig caagcccaaccctcttgagactggagctgagctcgcatacagagagactgg tgaacacttggtgctctgctgcacccctcgaacagaccacacttgggactgg gagctgggctggaagtgcctgacccatgacacccaggttgcgaattataaag agacaaactatttggtaactgacactgttctcgaacacagagagcagagaggg tcaatgactgttctatagactcgttgcacgtccacaaagaaacataccctatgta gttgaggattatgtaattatgtgaactgataataaactaaatgtctgctgactac cctgttgataaagataattgagagagctgtaacacaaagaaacataatcag cattctagcaaaatgctcagtagtgaattgctcaaaatacaatgttgattttagt cacttgccttataacatccttttctgtagatttcaataatgagtaattttagaa gcaattattttaggaataatagtgtaacagaaataatctgtttttctatgacattgta caaattttctccttctgttctgttggtgactcaacactaaactgt	4616	NM_015675	SEQ ID NO:90
HIF1A	"hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor) / hypoxia-inducible factor 1, alpha subunit (basic helix- loop-helix transcription factor)"	200989_at		aagcgaigtatctctcgtgaaagcagtggtctccacggaaacatggtgtggcta gcatctcttgatcgtatgacagatggtgtaaacacatcctgaattgtcttctg accacacccctccagtagaacttgccttataatccatttagcaatccagcctct gtgaaacataatagaggagaaagggaacacattctcttgaacttactcc ctaagctacttacttactgatacctaatacaatgatgtgagtgaaatacaga aggggtgttgatctcagatttcaataaacacacttcttggaaatagctgcaataa cttgaaagaagcctgttggtggcagaagacaga	3091	NM_001530 / NM_181054	SEQ ID NO:91
HOP	homeodomain-only protein / homeodomain- only protein	211597_s_at	+	gtctgtgtgtgtgcaaacctcactcaccacgcactcacacacgaacttctgtt ctccatgcaaaagttaaatacgaatccatccctgctgaggggaaaaaaagaaaa aaaatttaocagagaggggtctgtaactcgcagagacagcagcaatcgttct tctctgtcacttctccttagadtaataagcgttttggaaagtcggcagtagtctgt gtgtgtgtgtgacacacagacccacacacacacacacacacacacacacacac gtcgtctaaagatctgtagaactcgttattgactgcttctgtcttctccacccc tcttagcaccccccac aaacaaaaaataaaaaatagaacatagcaagcaagcaagcaagcaagcaagca cccaaatattgtctgtccctgtctgggaggtgtgtattttaaagatattctgtgtgt atctttgcaatgtagcttcttaaat	84525	NM_032495 / NM_139211 / NM_139212	SEQ ID NO:92
HOXC10	homeo box C10 / homeo box C10	218959_at			3226	NM_017409	SEQ ID NO:93

ITGB2	"integrin, beta 2 (antigen CD18 (p95), lymphocyte function-associated antigen 1; macrophage antigen 1 (mac-1) beta subunit) / integrin, beta 2 (antigen CD18 (p95), lymphocyte function-associated antigen 1; macrophage antigen 1 (mac-1) beta subunit)"	202803_s_at		atctggagggtctgatccacctgagcgacctccgggagtagacagcgctttgag aaggagagctcaagctccagctggaacaatgataatcccttttcaagagcgc caccacagcgctcagaaaccccaagttgctgagagtagagcacttggtgaa gacaaggccgtcagagccaccactgctgcccacatcagcgccgagacatg gctggccacagctctgaggaatgacacaaatgaacaaatccagttatccc gacctcaaatgacagccatgcccggccggtgcttctggggctcgtggggg gacagctcaactgactgacacagctttgcatggagagactgagggaggtga gggtggtaggtgaggtttctctgccaagt	3689	NM_000211	SEQ ID NO:94
KHDRBS 3	"KH domain containing, RNA binding, signal transduction associated 3 / KH domain containing, RNA binding, signal transduction associated 3"	209781_s_at		cagcccgccaggtggaggtgtagtaccacagaggagcgccaactccacaggg agctctgtccaccaggggccagtgagtcggggaagagagactctccacca gagcaagagaggtcccccactggtagacagactccaccccccacccga cacaaagagactatggagaatgactatgactatgagtgatagtcacitgat gaacagatgattgattctatgataacagctatagcccccacccaaagtggt gctgattactatgattacggacatggacacagtaggagagactatgattctacgg gcaagagagtgactaacctcaagacacagggcaacttcagcgagacagc aaagggtctacagagacccagccataltgccagatactgattgactctgagt ttgtgaatagccaatctccaccagctctgtatctg	10656	NM_006558	SEQ ID NO:95
KRT13	keratin 13 / keratin 13	207935_s_at	+	gagaacacgggtggcagagacggagtgccgctatgacctgacgtgcagcg atccagggactcactacgacgcatcgaggccacgctgagcgagctccgacgtg agatggagtgccagaaacacagagtagacagatgctgctggacataagacacg tctggagcaggagatgccaccctaccgacgctgctgagggccagacgcc aagaaagcgacgcccctgtagccctctgtaccacgactctagtcctctgta ccaccactctaaagctctgctgctgacgacccagagtaggagccctaaatct gacctggctccctccctctgctgctgacgacccagagtaggagagccggca gttccctcaggaagagaggggctgctggaccccaaggctcagacctctgct ctcaggacccctgctcactctctgctgagtggtggccctctgctctctcc ggctgactctctctctgacctggagacgcttggtttctcaacttc aacftlaacttagagctcattacttaagaatgaaacacacccctgagttgattt cccaaaagttaataaagcccttaagctcatgatttcaacactcttgccacata gtcatttacctccacagccgttggctcagtagaagggtgggtggttggattgat tttttcaactcagtgagaataatagtaggggacaaaacttactgtttcttaag acaattcagtgctgagcatctctgcaagaatggaatgaaatcagtagccaat tagaatatttatgatttatgtgttctgctgattttttatgaaaataataattatcatt ctgactctctggaagcaa	3860	NM_002274 / NM_153490	SEQ ID NO:96
LASS6	LAG1 longevity assurance homolog 6 (S. cerevisiae)	212446_s_at	+		25378 2	NM_203463	SEQ ID NO:97

LTBP2	latent transforming growth factor beta binding protein 2	204682_at	gagagcaaggctttatcagclaaagaaatattcagtagctgaalccgcacaglgatagccctgggcaaccagcagcaaggccgtgccalgggatalacagaccca tctacaagaccctctattacataaacacgtctctacaggaacaaacccctctctg ggatcccttttgtaaaacacagtttgatgctaaagaaagaaagctatctccag tgtgtctgttcagagcagcagagttccaatgtgttttccctccacccagaa acccctgcccctccctcagaaacagatggcaggccattccctgagttacaaagc agagacccaccccaacccagcagcggg acacacacatgcaattgtctaacaaaagtatttataacagtttcalacagaa ttaccitaaaaggagctctatgtttcaacacacagatagttgaaggatontaca gaagataatgatagtagtgaaatattctagaagggtgtgtctgagctgtgc taccatgctatgtattctgcaagcagataaaataccgtgtattttcttaccata gggataatgcataaggaaatattctcatatataatccclaaatgacagggg ggaaatatttaattgcccatgataatgtattttactatctatgcacagaggaact ataaagtaattacacatgtaactgtgttttccacataatgaggtatctttgagta gggtgaagaaagaaaaaattattaaatgaattgaattccctgatggatagta aat	4053	NM_000428 / NM_032035	SEQ ID NO:98
MAP4K5	mitogen-activated protein kinase kinase 5	203552_at	gaactcgtcatctcaltggttacaagaaatgtgcaggcagccagcagtagatt ccattcaltgaacacacagttggagagagataccgttttagtgtttgacaaattgt gaaaattgtaaatctacaaggaataaaatacaaglaagaaacgtggtcttga gttaagtttgatttcgattgaaltctgtatgtatgctcaagacagtggtgttctt tggaacatggagtgagggglaaaagctcaagctcagatgaggttacaacagga gatttcagatgaacacagagtttccgttattaggtacacacaggggtgtcttttg gaaatgaggcccaacagaaatccctacgtcacacacagcaatctctacatctgct ggacatgaaaatagttactaagcaacagaaactgaltcacaalgcacaggaaa atgaatatactccaltgaaagggaataaggaataatcaatacaaacctgcacta tgatttgccttaact	11183	NM_006575 / NM_198794	SEQ ID NO:99
MAP4K5	mitogen-activated protein kinase kinase 5	203553_s_at	ctcagagccacccctaaagaatcctttagattttcaacgcagccctgtttggg ctgcccgtgtgtgccacactcaggctctctcttccacaaactctgtgtgtcac agaaaccttgagcgaatggagactgtctcaagaggggcacgtgtgtgtccac agcctggcacagggcagtgaggacagggcaggtgcccaggtggccactccagac ccctggctttcacgtggtggtccttagaaccttcttcaatagcaggttctgtgtat gcacttgtttttctttgtgtgtgtgttttttccacttagaaattgcatttctgcacaga aggactcaggtgtgtgaagctcagcagctgcacatcctcagccccacatagtgatg gttcccdgttccacttactagcatgtccacacagcaggtctcttccacgtgagga ggaaaaccaaagccgtgtgtccctccagccctccctgtccctccctccacccat tcccacatggggaat	11183	NM_006575 / NM_198794	SEQ ID NO:100
MMP2	"matrix metalloproteinase 2 (gelatinase A, 72kDa gelatinase, 72kDa type IV collagenase) / matrix metalloproteinase 2 (gelatinase A, 72kDa gelatinase, 72kDa type IV collagenase)"	201069_at		4313	NM_004530	SEQ ID NO:101

MYC	v-myc myelocytomatosis viral oncogene homolog (avian) / v-myc myelocytomatosis viral oncogene homolog (avian)	202431_s_at	+	gcaacacccgaaatgcaccagcccggtctcggacaccggaggaatgtcaagaggcaacacacacacgctctggagcccgaggaaggaacgagdaaagcggtctttttgcctcgtgacagatcccggtggaacacatgaagagccccaaggtgattatcccttaaaaaaagccacacatactcgtccaaagcaggaagcaaaagctcttctgaagaggctgtgcgaaacgacgagacaggtgaaacacacactgaacagctacggaactctgtggttaaggaaaglaaggaacacgctctcctaacagaaatgtctgagcaatcaccctatgaactgttcaaatgcattgatcaaatgcaacctcacaactctggctgagtc	4609	NM_002467	SEQ ID NO:102
NRP1	neuropilin 1	210510_s_at		aacatccgcctgglaacacgctcgtctggctgggcacttccacccgacactcctacatcaatgagtgctccaalagacctgggggaggaagagagctgaggggcatcatcattcaggtgggaagcaccgagagaacaggtgtcatgaggaaglicaagatcgggtacagcaacacgctcggactggaagatgcatggatgacagcaaacgcaagcggaaggtctttgagggcaacacacatgatataccctgagctgggacttccagctctccacggaatcatcaggatcaccogaagagccactcatggcggactgggctcagaatggagcgtgggctggaagtgaagccctacagctggaccacactccacacggggaactgtgggaatgtgtgagcgaccagggccaactgcccacagtggaaca	8829	NM_003873	SEQ ID NO:103
NRP1	neuropilin 1	212298_at		gcaaatctctacacagcgagcctatgaalttaaccccaagaagactttgtgtttgtgtgattttatcagcctgttgacatgagatttttagatctcttccacactgctagcgtctcactcaagacatttgtgggagctcacttgcatacagangagacagctcatctctgtaaatgtgattgagaaatgctttgttccaggaaatattgataccatgaagaaatgtttttgtcccaagagacatttattgtatataatctaccagaggaagcaactaagaacacactgtgtgttttaaggcaacagactiaaaggtgtcctcagccaagg	8829	NM_003873	SEQ ID NO:104
OLF1	olfactomedin 1 / olfactomedin 1	205591_at	+	cagggtgtatctgcacagtggtcgcacacagcagaccatgttccacgggagccgcacaaaacagctgagggcagctactggagaggtgcaagaacatgctcaatccatagaggtcttgacaggcgacccagagacactgcaactgagagaaatgaggaacccaatgaagggactggagctcaggtcacaacagggggaggaagatataagcaacacctggccagcgatgaagggttaactaaagagttttcaatgctgcagtgacggaagagcgtccactccatgtaacctgaagagagccagagagcttttgcacctgcatcttactattttccaactagaaccacttccctaaaggaaactgaatacaccaggatcctcttgcactgactgtagctgc	10439	NM_006334 / NM_014279 / NM_058199	SEQ ID NO:105
OLF1	olfactomedin 1	213131_at	+	gcgggcacagacgctcgggaagaaactccglatttgcagctggaactgcagccacggcccggtttctccgcgccttccctctcctggtaacacacatactaaagagcgagggaatgactgtgtggcaggtctcaccggggaacacccnactgttaggtgacatgaacatttcttagatcgtgtcagctccgaggaatgtggcnncacagctcttgangagccatgggctcaccnnggctgagggctatgtgtaacagctcattgcagtgccngtctnigtactgtgtgtgtctcttagataacogtgcctgaggtcctnatactagctcctnigtgacctgtgtctnatactagactgaagcgatggtaaggtgtgtagaggaagtgtgtgcccacatgtttgaaactcgtgtaaccccgtagatacatgtgcaacgttctctgttattccttgcaggtgtgactcgtatgttc	10439	NM_006334 / NM_014279 / NM_058199	SEQ ID NO:106

[illegible]

PLAU	"plasminogen activator, urokinase / plasminogen activator, urokinase"	211668_s_at		accacaacgacattgcttctgtgaagatccgttccaaaggaggagggcaggtgtgag cagccatcccgacatatacagaccatctgctgcccgcgctgataagatcccc agttggcacaagctgagatcactgacgtgcttggaaaagagaattctaccgacta tctctatccggagcagcagagatgactgttgaagctgatttccccccggaggt gtcagagccacactacgctctgagctgagctgacacacacaaatgctgtgctg ctgacccacagtggaacaacagattctgcccagggagagcactcaggggacccct cgctgttccctccaaaggccgctgactgactgacagagagctcactc gattgcccgtgaagagcagcagcgtctacacgagagctcactc gggtgcccattccaaaggaaagcttcttgcacaaagggggacagtcagtttgc aaaaggagctcacttactgttaataatgtctcctaatgggataatttaatacaaa gattgactagaagtgaaactgcaacactaacctcccggctgtgtgtgactcg agttgtgacacagccacagacacccagagctggcttggaaacacacactca gggtttgtgaaaggttccccgctgagatcttctctctgttactgtgaagcctgtt gggttgcgtgtgttggaggagggccacagggggagagcagtgacgtgacccg ggacacacccactgactgagctgtgctcagacaaatgtaattctgtgtgtaaca gaaagtggcctgtaagctcctgtcctcggaggagagcattctgtgtggtttg gctgaaggcagatgctgccaaagacagctgagaactcagagccctgtgca ctgtgtgagaagggttctggctacaaaaggctccactccacaggggtgactctc ctcactgtgccaggcggtgctcactcaccacacacacatggcacaggcgggaagt ccatctacggagcgccttctgacgagaacttactcactgaagcactgtgggc cagggtgtctgtccatgctlaalgtgtgtcctacacacacacaggtccactctc atctgacccataagagacagctgtgtgagtggaagcactgtgtgtgctgacgt caaaaggcagtgagcgtggaagaaalagaatcttctggctctaaagagtg ggagacatccaaagagattgtcatcacagactgtggccaggtgagcactgtg ggccagggtgtgtgctgtgtggaagctgcaaatgtccatgacccagggtggcc gggttgggctgtcagcccaagggtgctgaaacgagacgtgtgcccact	5328	NM_002658	SEQ ID NO:115
PPIF	peptidylprolyl isomerase F (cyclophilin F) / peptidylprolyl isomerase F (cyclophilin F)	201489_at		gggtgcccattccaaaggaaagcttcttgcacaaagggggacagtcagtttgc aaaaggagctcacttactgttaataatgtctcctaatgggataatttaatacaaa gattgactagaagtgaaactgcaacactaacctcccggctgtgtgtgactcg agttgtgacacagccacagacacccagagctggcttggaaacacacactca gggtttgtgaaaggttccccgctgagatcttctctctgttactgtgaagcctgtt gggttgcgtgtgttggaggagggccacagggggagagcagtgacgtgacccg ggacacacccactgactgagctgtgctcagacaaatgtaattctgtgtgtaaca gaaagtggcctgtaagctcctgtcctcggaggagagcattctgtgtggtttg gctgaaggcagatgctgccaaagacagctgagaactcagagccctgtgca ctgtgtgagaagggttctggctacaaaaggctccactccacaggggtgactctc ctcactgtgccaggcggtgctcactcaccacacacacatggcacaggcgggaagt ccatctacggagcgccttctgacgagaacttactcactgaagcactgtgggc cagggtgtctgtccatgctlaalgtgtgtcctacacacacacaggtccactctc atctgacccataagagacagctgtgtgagtggaagcactgtgtgtgctgacgt caaaaggcagtgagcgtggaagaaalagaatcttctggctctaaagagtg ggagacatccaaagagattgtcatcacagactgtggccaggtgagcactgtg ggccagggtgtgtgctgtgtggaagctgcaaatgtccatgacccagggtggcc gggttgggctgtcagcccaagggtgctgaaacgagacgtgtgcccact	10105	NM_005729	SEQ ID NO:116
PPIF	peptidylprolyl isomerase F (cyclophilin F)	201490_s_at		gggtgaatgttgccttaggataggcctatgtgtcagcccacaaagaatattgtctc attagcctgaatgtgccataagactgaccttttaaaatgtttgaggatctgtgat gctgttaattgtcagcccaatttattgagaaatattctgtgtcagcactgtg ggtttaatttttaaalcaaacgctgattacagataatgatttataataaaitg aaaaaaatttcttgggaaggaggaagaaalgaataaataatcattaaagata actcagggaatctcttactaatttacgttttagaattgtttaaggttaagagaaga tagtcaalatgctgtataaaacactgtcacactgttttttaaaaaaaactgattt gttataacattgactgtgtgacaaaacctgggaatttgggtgtgtatgcaagtgtt cagtgccctcagacaaat	10105	NM_005729	SEQ ID NO:117
PTGS2	prostaglandin- endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase) / prostaglandin- endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	204748_at	+	gggtgaatgttgccttaggataggcctatgtgtcagcccacaaagaatattgtctc attagcctgaatgtgccataagactgaccttttaaaatgtttgaggatctgtgat gctgttaattgtcagcccaatttattgagaaatattctgtgtcagcactgtg ggtttaatttttaaalcaaacgctgattacagataatgatttataataaaitg aaaaaaatttcttgggaaggaggaagaaalgaataaataatcattaaagata actcagggaatctcttactaatttacgttttagaattgtttaaggttaagagaaga tagtcaalatgctgtataaaacactgtcacactgttttttaaaaaaaactgattt gttataacattgactgtgtgacaaaacctgggaatttgggtgtgtatgcaagtgtt cagtgccctcagacaaat	5743	NM_000963	SEQ ID NO:118

RRM1	ribonucleotide reductase M1 polypeptide	201476_s_at	+	6240	NM_001033	SEQ ID NO:119
SEMA3B	"sema domain, immunoglobulin domain (lg), short basic domain, secreted, (semaphorin) 3B / sema domain, immunoglobulin domain (lg), short basic domain, secreted, (semaphorin) 3B"	203071_at	+	7869	NM_004636	SEQ ID NO:120
SERPINE 1	"serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1"	202627_s_at		5054	NM_000602	SEQ ID NO:121
SERPINE 1	"serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1"	202628_s_at		5054	NM_000602	SEQ ID NO:122
SLC20A1	"solute carrier family 20 (phosphate transporter), member 1 / solute carrier family 20 (phosphate transporter), member 1"	201920_at		6574	NM_005415	SEQ ID NO:123

[illegible]

[illegible]

TIMP3	"tissue inhibitor of metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory)"	201150_s_at		gacatttggaaatagccctgctagggcaaacctgaggcccccagggagacacaccc cttccatgccccagacccctgctgcatgagacaattgacaatctggactacccc aagatggccacccagctggttggcttctgctaccacaaagggttaacatgctacagag tatattttagagacacaacataaataatcgtatggcaaaagcaaaacataaat ggaagtaggggaggtggaatggacaacacgtccaaattggctcttggagcc gagagaaaggaggacactggagaatgttttcttgggggagagggctctt agattccccagcatccgcttccctttagccagctgctgctgaaacccagaa gtgatggagagaaacacacagagatcgcgaacccctgctaggaaggaaatglat ttgtgctaaatttctgagcacgttaccagttttccatctccatgttattatg gagttactagagcttggccacctctccatttttggcttggctctcatctaatggcct aatgcaccccaacacatggaataatcacaacaaataacttaatagttccaccaa aaggcaagactgacctagaaatctagccctggttggagatactaacctgctctca gagaaatgagcttggacatgcatgaacccatgttgcataaagatgataa aataatctatttcccccaccccgaaatgtcaaatgtcccatgttaaaac ctgctacaatggagcttatacagaaatgtcaaatcatctcgtatttagg aatgctctgcatcccccaaggttctaaagttaagattctctactactactca cgtttaaatcttgaagattgtattaaatggaatttgaagaaataattattatttc tgaatatgtaaacctggaagatgataaacctgaagcagataccctggaacccac ctaaagaaactccattatggagatttttggcccttggcttggattat accaaagttctcatgaatccacacttaaatctgaacagctggcaataataattta tctgattgactgagtaaatatataccacactatgctggagctgacacdaagtc aagttaaaggcttggtaaaagaaatggttgcataatgaagcaaaatagataga tcaagaatgaaatgtccaaagacacagacagaaacagaaatgtaacatgctgt aatggcatcaactcagaaagaaagagcgatgacacattgataaagat ctcaaaaaggaactcttctgctgagagaaatcagacatcatcctcaa ggacattactagctgactcagaaatcactcagaaatgaatccaaagct ggctagagtaaaacacacaaatcagctgctgataatgcaattagtttgan aagattcttaataagctggctgtaataactgcttgggtt gtagcagctacataactgggcccagaggaaggaagcaacacatgctctctcc aaactccaaagaatgaaaaggcttggccgcacaaataaaactctgggaatcat caaggatgggaattctctgagcaactgacatgaggaatggggaactggt catcatgaaaggggtttactacatctatcccaacacacttctgatttcagga ggaaataaaagaaacacaaagacagacacaaacaaatggccaatataattac aaatacaacagattactcctgaacctatttgtgtagaaaagtgtcagaataatgtgt tggctaaagatgagagaataggactctatccatctatcaagggggaatttga gcttaaggaaaatgacagaattttgtttctgtaacaaatgagcactgatagacat ggaccatgaagccagttttctgggccccttttagtggcctaactgacct ctctacctatatacgttgtcagcagaataatctaggaagactgtcagcttccaaaca ttaatgcaatggttaacatctctgtcttaatactactccttgaagaagactgtagaa gaaagcgcaacatctctcgaagtgtgatacagatgtagctccagggt tcttaaggggacaacatccttaagtaaaaaagagagaagagggaacacataaaa gactccagtttgcctggtcagctggc	7078	NM_000362	SEQ ID NO:134
TNFRSF6	"tumor necrosis factor receptor superfamily, member 6"	204781_s_at	+	NM_000043 / NM_152871 / NM_152872 / NM_152873 / NM_152874 / NM_152875 / NM_152876 / NM_152877	355	SEQ ID NO:135	
TNFRSF6	"tumor necrosis factor receptor superfamily, member 6"	215719_x_at	+	NM_000043 / NM_152871 / NM_152872 / NM_152873 / NM_152874 / NM_152875 / NM_152876 / NM_152877	355	SEQ ID NO:136	
TNFSF10	"tumor necrosis factor (ligand) superfamily, member 10"	202687_s_at	+	NM_003810	8743	SEQ ID NO:137	
TNFSF10	"tumor necrosis factor (ligand) superfamily, member 10 / tumor necrosis factor (ligand) superfamily, member 10"	202688_at	+	NM_003810	8743	SEQ ID NO:138	

[illegible]

Example 4**RT-PCR Confirmation Studies**

In addition, the sequence of the RT-PCR primers used in the confirmatory follow up studies as highlighted in Figs 3, 4, 5 and 6 are listed in Table 3. Note that DAPK2 was not identified by Affymetrix analysis, only via follow up of the DAPK gene family by RT-PCR following discovery of predictivity of DAPK1. Hence no Affymetrix ID or Affymetrix ID sequence is provided for DAPK2.

Table 3

Sequences relevant to genes followed up by RT-PCR (see Figs 3, 4, 5 & 6)

(all sequences written 5'-3')

Gene	affy id	affy probe seq	Taqman Forward Primer	Taqman Reverse Primer	Taqman probe
EMP1	201324_at	CACCAAATTACCTAGGCTGAGGTTAGAGAGATTGGCCAGCAAA AACTGTGGGAAGATGAACTTTGTCATTATGATTCATTATCAC ATGATTATAGAAGGCTGTCTTAGTGCAAAAACATACTTACATT TCAGACATATCCAAAGGGAATACTACATTTTGTAAAGAGTT GAACTATGACTGGAGTAAACCATGTATCCCTTATCTTTACTT TTTTCTGTGACATTTATGTCCTCATGTAATTTGCATTACTCTG GTGGATTGTTCTAGTACTGTATTGGGCTTCTTCGTTAAT	AGCCATCCTG CCCTTCTGA	ACCTTACAAAC TCTCTTTCC	CAAAGCA AAACATC ACATTCC AGTC
NES	218678_at	GCAGCACTCTTAACCTACGATCTCTTGACATACGGTTTCTGGC TGAGAGGCCCTGGCCCGCTAAGGTGAAAAGGGGTGTGGGCAA AGGAGCCTACTCCAAGATGGAGGCTGTAGGAATATAACCTC CCACCTGCAAAGGGAATCTCTTGCTGCTCCATTCTCATAGG CTAAGTCAGCTGAATCCCGATAGTACTAGGTCCCTTCCCTCC GCATCCCGTCAGCTGGAAAAGGCCGTGTGGCCCGAGAGGCTTC TCCAAAGGGAGGGTGACATGCTGGCTTTTGTGCCAAGCTCA CCAGCCCTGCGCCACCTCACTGCAAGTAGTGACCATCTCAC TGCAGTAGCACGCCCTCCTGGCCGTCTGGCCTGTGGCTAAT GGAGGTGACGGCACTCCCATTTGTGCTGACTCCCCCATCCCT GCCAGCTGTGGCCCTGCCTAGTCCCTGCCTGAATAAA G	GCCCCTTTCA GCAGGAGGA	AGTGCCGGGG AGATGCTCTT	AGTGCTC TGAAGAC CTCTTGG GC
DAPK1	203139_at	CCTCCTCCAGGGTGATTTTATGATCAGTGTTGTTGCTCTAGGA AGACATTTTCCGTTTGCTTTTGTTCGAATGTCAATGGTGAACG TCCACATGAAACCTACACACTGTGATGCTTCATCATTCCTCTC ATGTCAGGTAGAAGGTTGACACAGTTGTAAGGGTTACAGAGAC CTATGTAAGAATTGAGAAACCCCTGACTCATCTTTGTGGCA GTCCTTATAATTGGTGCATAGCCAGATGGTTCCACATTTAG ATCCTGGTTTCATAACTTCCTGTACTTGAAGTCTAAAAGCAGAA AATAAAGGAAGCAAGTTTTCTTCATGATTTTAAATTGTGATC GAGTTTTAAATTGATAGGAGGGAACATGTCTAATTCTTCTGT CCTGAGAA	AGBAAACGCT ACCTCTCTGT	CTGGAGGAGG ATTCCTCTCT	CTTGCTG TATGCTG ATCATCG CC
DAPK2	Not applicable	Not applicable	GGGTAGGCAC CTGGCATC	AGTGCAGTGG CGTGATCTC	TACTCCA GGGGCT GAGGTGA CA

Example 5

Diagnostic test for Clinical Studies

The predictive gene lists above have been generated using the preclinical studies described. The following approach is employed to develop a diagnostic test for the clinical setting based on this data.

- a) Identify patients which represent the population of individuals whom we would expect to derive benefit from a diagnostic test, and for which pre-treatment tumour samples and outcome of gefitinib treatment are known or will be available. For each sample the expression level for our genes of interest is evaluated, using for example the RNA signal from RT-PCR. QC procedures are applied to identify the set of samples and genes to take forward to step b).
- a) Identify a subset of the genes which together are able to distinguish between patients showing different responses to gefitinib. There are a variety of methods which are useful to select the subset of genes and combine their expression values to provide a prediction, possibly a predictive value and a corresponding threshold which distinguishes between different patient groups. An example is stepwise Linear Discriminant Analysis where genes that distinguish well between patient groups are successively added to a linear combination until addition of a further gene does not provide additional predictive power (Mardia et al.). The threshold value of the linear combination is then selected to give the appropriate sensitivity and specificity properties.
- d) Tool validation would partly be carried out during development in step 2, for example using cross validation and permutation tests. In addition, the finally developed diagnostic procedure (gene subset and method of combining to generate a prediction and a platform for biological analysis) is tested and validated in its entirety using an independent set of samples not used within tool development in step b).

References

- Bailey et al Lung Cancer (2003) 41 S2 , S71
Downward et al. (1984) Nature, 307, p521
Fukuoka et al (2003) J. Clin. Oncol., 21, p2237
Kris et al. (2003) JAMA, 290, p2149
Lynch et al.(2004) New England Journal of Medicine, 350(21) p2129

- Mardia K.V., Kent J.T., Bibby J.M. (1979) "Multivariate Analysis" London, Academic Press Inc. Ltd.
- Paez et al. (2004) Science, 304 p
- Salomon et al. (1995) Crit. Rev. Oncol. Haematol, 19, p183
- Scheffe, H. (1959) "The Analysis of Variance" New York, Wiley
- Sporn & Todaro (1980) New England Journal of Medicine 303, p878
- Storey (2003) "Statistical Significance for Genome Wide Studies" PNAS, vol 100, issue 16, pp 9440 – 9445
- Yarden & Sliwkowski (2001) Nature Reviews Molecular Cell Biology, 2, p127

CLAIMS

1. A method of selecting a mammal having or suspected of having a tumour for treatment with an erbB receptor drug which comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 1 or DAPK2, whereby to predict an increased likelihood of response to the erbB receptor drug.
2. A method according to claim 1 comprising testing a biological sample from the mammal for expression of any one of NPAS2, NES, CHST7, DAPK1, ACOX2, GSPT2, TNNC1 or DAPK2.
3. A method according to any preceding claim comprising testing a biological sample from the mammal for expression of any one of NPAS2, NES, CHST7 or DAPK1.
4. A method according to any preceding claim comprising testing a biological sample from the mammal for expression of at least two of NPAS2, NES, CHST7 or DAPK1.
5. A method according to any preceding claim comprising testing a biological sample from the mammal for expression of at least three of NPAS2, NES, CHST7 or DAPK1.
6. A method according to any preceding claim comprising testing a biological sample from the mammal for expression of NPAS2, NES, CHST7 and DAPK1.
7. A method according to any preceding claims additionally comprising testing a biological sample from the mammal for expression of any gene listed in Table 2 as defined herein.
8. A method according to claim 7 comprising testing a biological sample from the mammal for expression of any one of EMP1, SLC20A1, SPRY2 or PGM1.
9. A method according to any one of claims 7-8 comprising testing a biological sample from the mammal for expression of EMP1.

10. A method according to any preceding claim wherein the tumour is selected from the group consisting of leukaemia, multiple myeloma, lymphoma, bile duct, bone, bladder, brain, CNS, glioblastoma, breast, colorectal, cervical, endometrial, gastric, head, neck, hepatic, lung, muscle, neuronal, oesophageal, ovarian, pancreatic, pleural membrane, peritoneal membrane, prostate, renal, skin, testicular, thyroid, uterine and vulval.
11. A method according to claim 10 wherein the tumour is selected from one of non-small cell lung, pancreatic, head or neck.
12. A method according to any preceding claim wherein the erbB receptor drug is selected from any one of gefitinib, erlotinib, PKI-166, EKB-569, HKI-272, lapatinib, canertinib, AEE788, XL647, BMS 5599626, cetuximab, matuzumab, panitumumab, MR1-1, IMC-11F8 or EGFR11.
13. A method according to claim 12 wherein the erbB receptor drug is gefitinib.
14. A method according to any preceding claim wherein the mammal is a human and in which the method comprises testing a biological sample from the human for increased expression of DAPK1 and decreased expression of NPAS2, NES, CHST7 and EMP1 whereby to predict an increased likelihood of response to gefitinib.

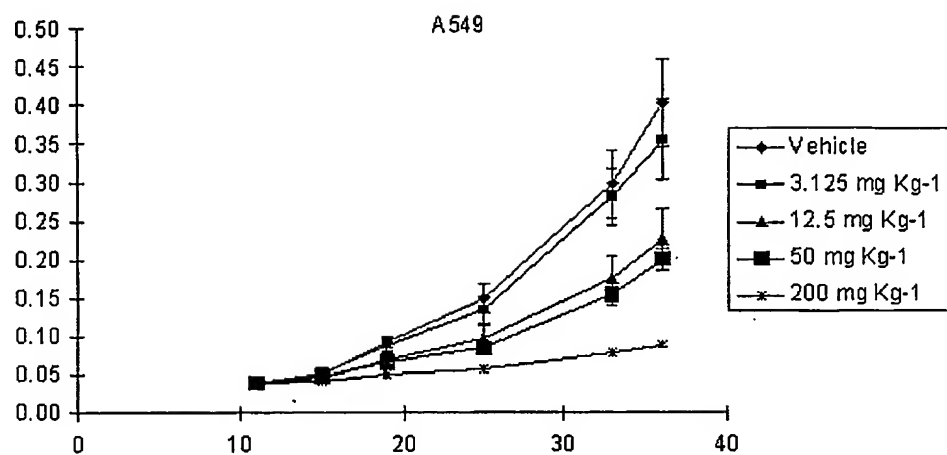
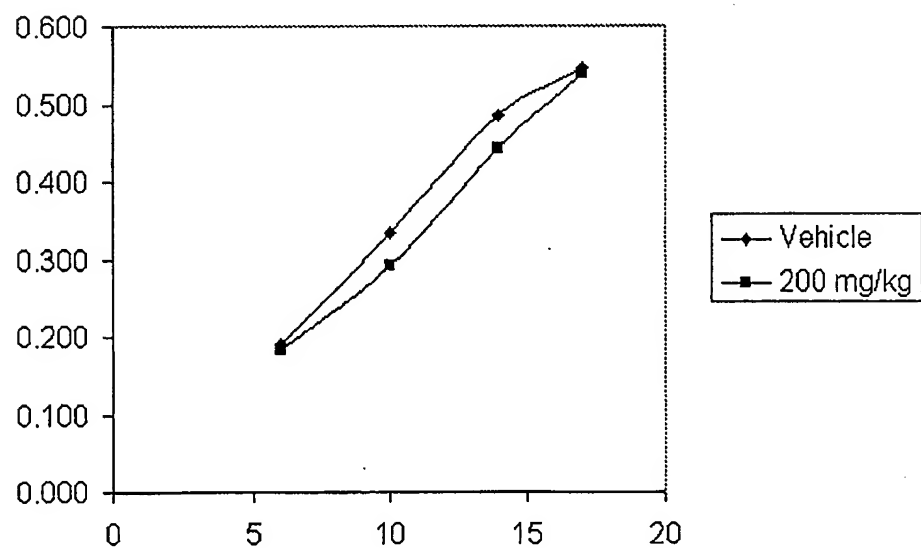
Figure 1**Figure 2**

Figure 3

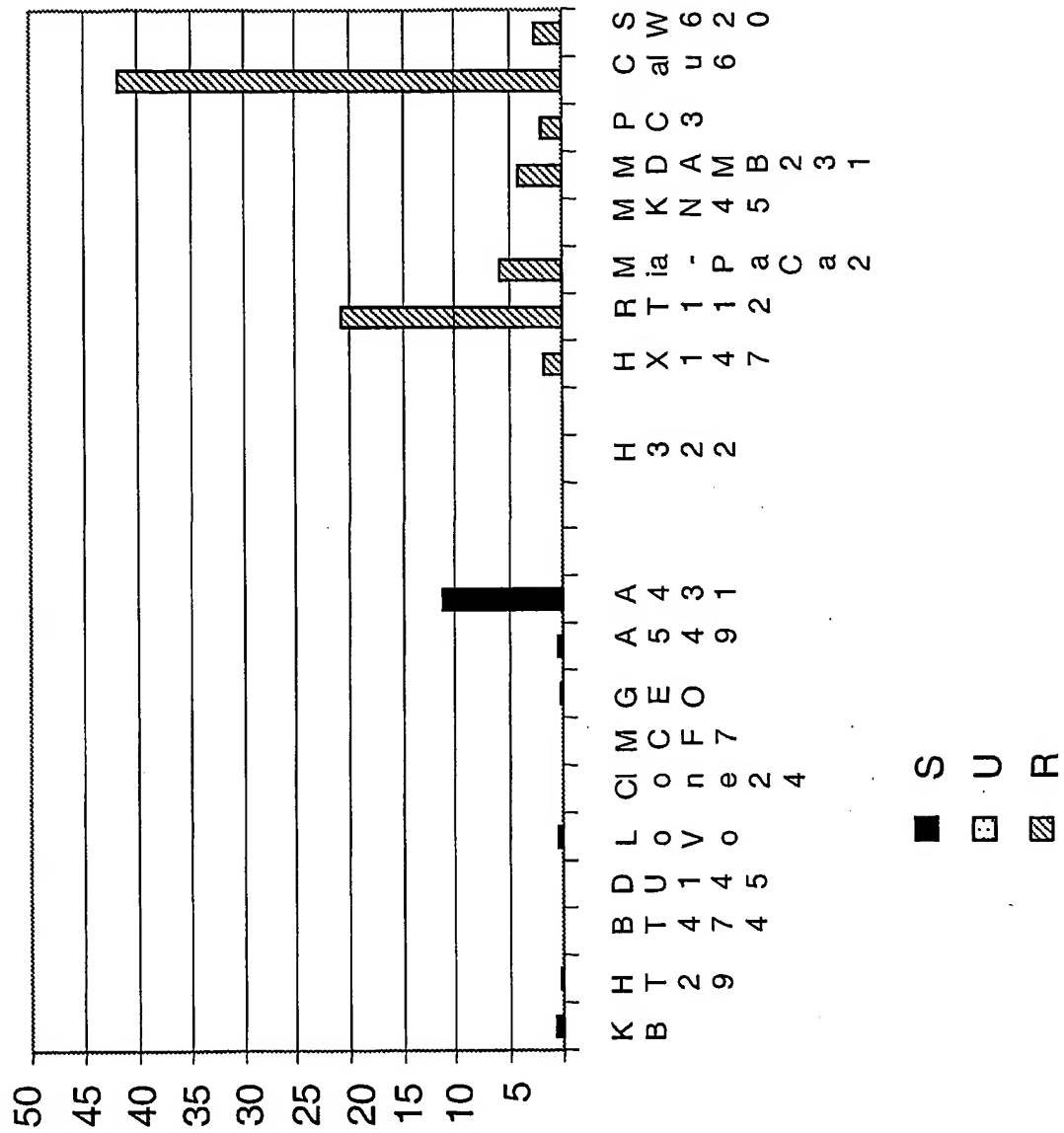


Figure 4

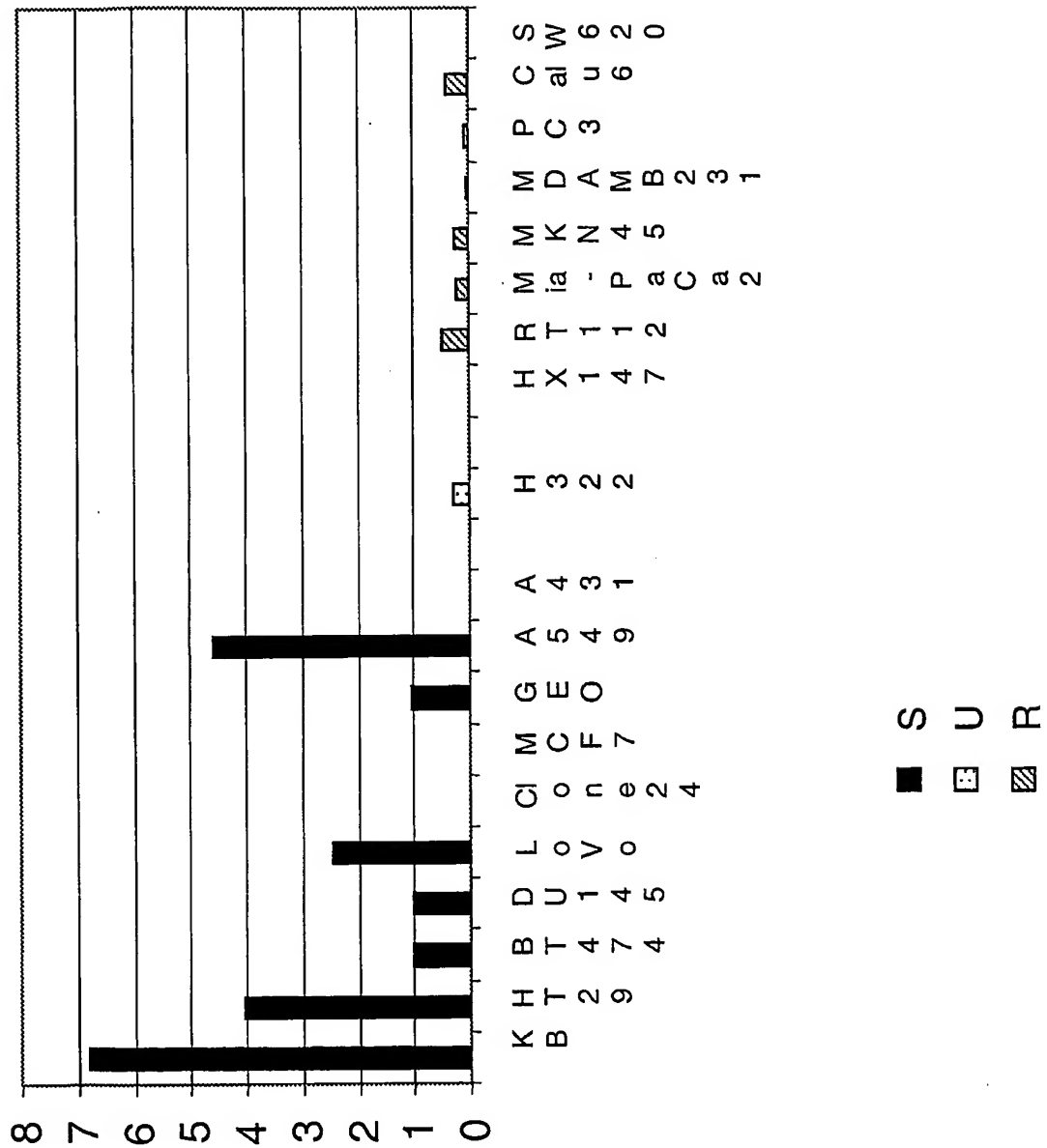


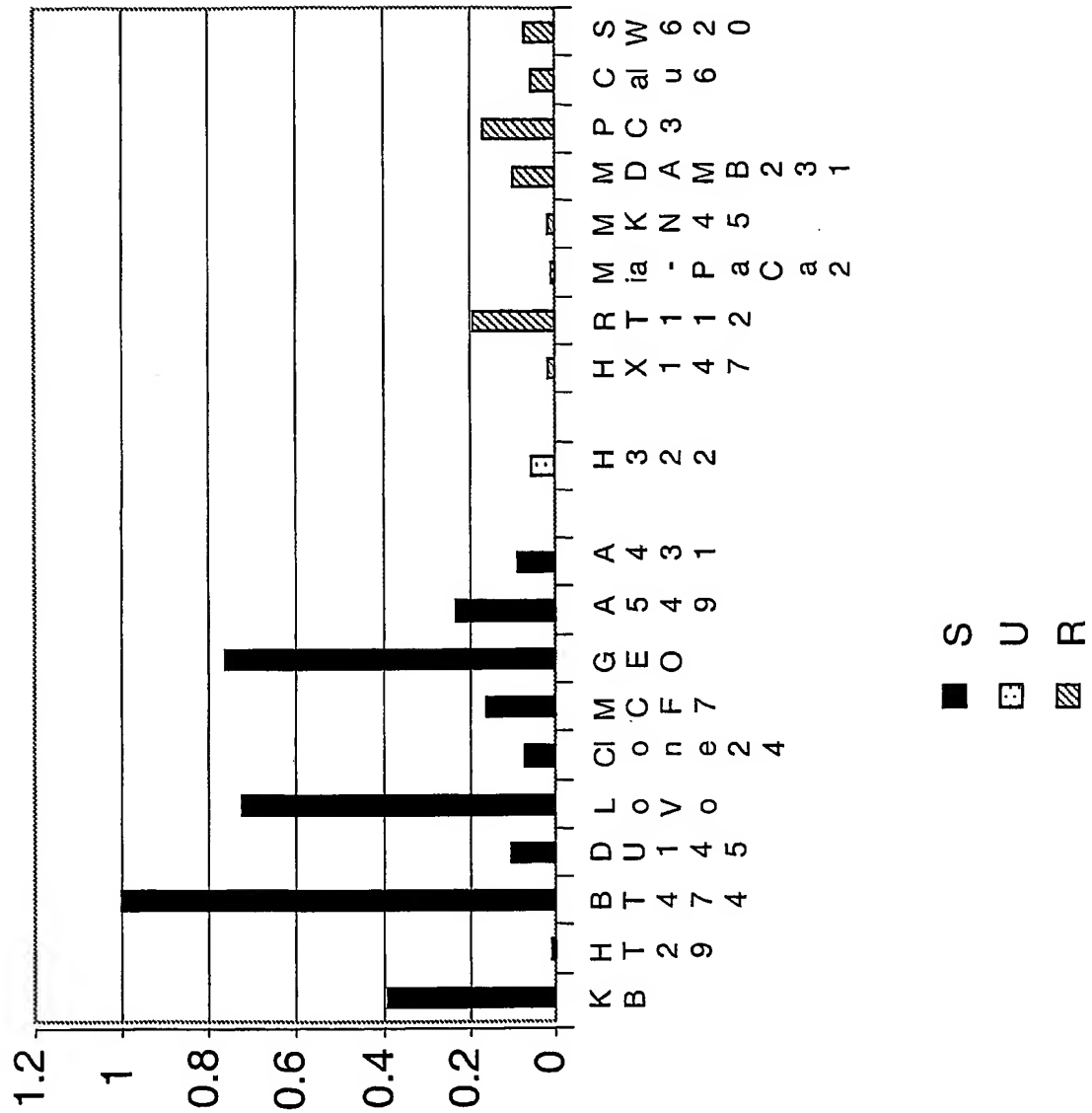
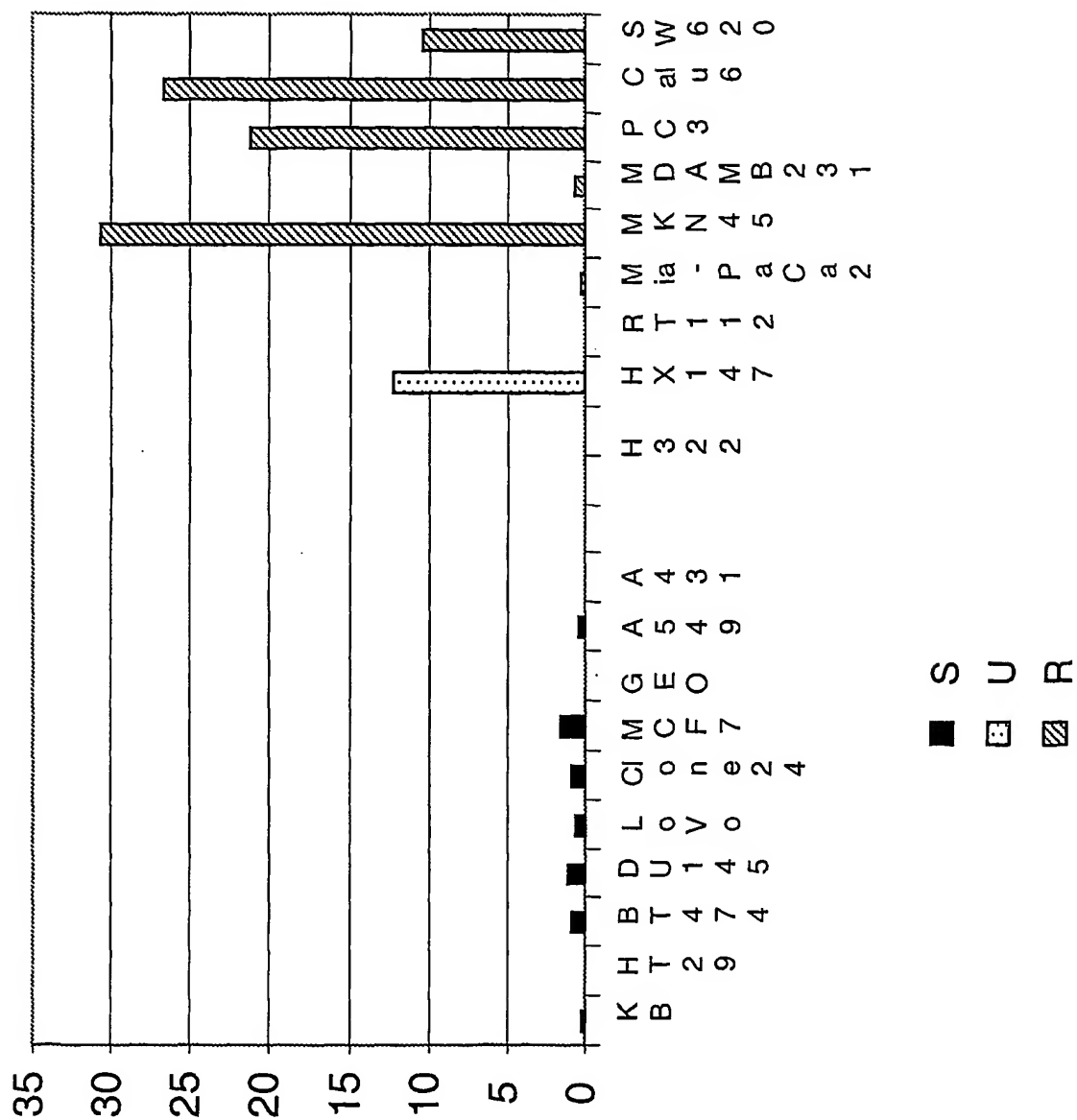
Figure 5

Figure 6

1

SEQUENCE LISTING

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<141> 2004-07-23

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<151> 2004-07-23

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gccttctctgt ctggtgccca agtggacatg gcaagaacag cctacctgga cctgctccgc      300
ctgatccgga aggatgccat cctgttaact gatgcttttg acttcaccga tcagtgttta      360
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<210> 2

<211> 507

<212> DNA

<213> Homo sapiens

<400> 2

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acaagcaggt acttacaaat aattactggc agtaggttat aattggtggt ttaaaaataa      180
cattggaata caggacttgt tgccaattgg gtaattttca ttagttgttt tgtttgtttt      240
gatttgaaac ctggaaatac agtaaaattt gactgtttta aatgttggcc aaaaaaatca      300
agatttaatt tttttatttg tactgaaaaa ctaatcataa ctgttaattc tcagccatct      360
ttgaagcttg aaagaagagt ctttggtatt ttgtaaacgt tagcagactt tctgcccagt      420
gtcagaaaat cctatttatg aatcctgtcg gtattccttg gtatctgaaa aaaataccaa      480
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<211> 348

<212> DNA

<213> Homo Sapiens

2

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tacagaccca gcccaggtt caatgtcctc cgaagaatga agtctttccc tggatgatgt 180
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<210> 4
<211> 487
<212> DNA
<213> Homo Sapiens

<400> 4
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gcatggtcag ggtccagct gtaggtgaga gcagggcact gtccagctgt ccaactgggga 180
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tgtgttt 487

<210> 5
<211> 318
<212> DNA
<213> Homo Sapiens

<400> 5
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ctcttcogtt cattcaatta ttttaagcat ttgaattatt tattgtatat cctaaatata 180
tttctccttt ggcagtgact agatttccac taatgtgtct taatctatcc ctccagctgg 240
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ctgtatccct tggagtaa 318

<210> 6
<211> 135
<212> DNA
<213> Homo Sapiens

<400> 6
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acacacattg aaaat 135

<210> 7

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<211> 402
 <212> DNA
 <213> Homo Sapiens

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 cagcatctct cggacggagg ccgctgacct ctgcaaggct ttcaatagca ccttgcccac 180
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<210> 8
 <211> 417
 <212> DNA
 <213> Homo Sapiens

<400> 8
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 gcagaacctt tccaaaagtt ttatatagag attcataaca acaccaagaa ttgattttgt 180
 agccaacatt cattcaatac tgttatatca gaggagtagg agagaggaaa catttgactt 240
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 atagatatgt ctttgtgtaa atcatttggt ttgagttttc aaagaatagc ccattgttca 360
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<210> 9
 <211> 546
 <212> DNA
 <213> Homo Sapiens

<220>
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 <222> (104)..(104)
 <223> n is a, c, g, or t

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 ttattttata tagtctggag aaaaaacaca ctgtaatatt tcaagtgtat gcagtagaat 180
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 gtgtctgtgt ttgttttaaa agtcacttat ttcttacagt gatttcaatt gcaccatgac 480
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 cttgac 546

<210> 10
<211> 546
<212> DNA
<213> Homo Sapiens

<400> 10
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taataatagg tctgggcagt attgttttta acctgactca tccagctgtc cttcaaatag 420
ctccgtctcc ctctaccag aactgatttt taaaaagaag taatttttct ccctgggctg 480
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gtaatac 546

<210> 11
<211> 496
<212> DNA
<213> Homo Sapiens

<400> 11
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atatttggtg accttaagtg tacagaacac tgattcccca tcctatccag agattagttt 180
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cgtgtgaaag ggtaagagg gaaagatact gcccaagtat ttgaatcgtt tagtagtaac 480
tgtccattta tcctat 496

<210> 12
<211> 313
<212> DNA
<213> Homo Sapiens

<220>
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<222> (190)..(190)
<223> n is a, c, g, or t

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ggctcttaca ttggtttatt caattgcatt ttttctaact cgtgtctcaa gtgtttttaa 180

5

aatctactgn acttataatg acttatataa tgtattttctc attttacctt tcttccaaaa 240
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 tttgataact tgt 313

<210> 13
 <211> 395
 <212> DNA
 <213> Homo Sapiens

<400> 13
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<210> 14
 <211> 569
 <212> DNA
 <213> Homo Sapiens

<400> 14
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 cctattttgat agaggaaatg tatgatgaag ctattcagga ttatgaaact gctcaggaac 180
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 atcccttcag ctcaggcgga ccatttaga 569

<210> 15
 <211> 481
 <212> DNA
 <213> Homo Sapiens

<400> 15
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6

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<210> 16
<211> 398
<212> DNA
<213> Homo Sapiens

<400> 16
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aatggcaata aggactccga atacataata aaagcaaaca gaacactcca acttagagca 180
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acagatccta gcaaatgtgc ccaaccagct ttactaaagg gggaggaagg gagggcaaag 360
ggatgagaag acaagtttcc cagaagtgcc tggttctg 398

<210> 17
<211> 499
<212> DNA
<213> Homo Sapiens

<400> 17
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tatgtgccgc cgagcctgcg cgacggggcc agccgccgcg gggagtccat gcagcccaac 180
cgcagagccg acgacaacgc caccatccgt gtcaccaact tgtcagagga cacgcgtgag 240
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<210> 18
<211> 261
<212> DNA
<213> Homo Sapiens

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<221> misc_feature
<222> (41)..(42)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (196)..(196)
<223> n is a, c, g, or t

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 agggtaaagg gctatnggca acaggggacc agaccaggga tgagtgggga gggcacaagg 240
 accatttgcc agaatccacc g 261

<210> 19
 <211> 526
 <212> DNA
 <213> Homo Sapiens

<400> 19
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 agagcgggag ggagtctcag gaggaggett gccctgaggg gctggggagg gggtaacctca 180
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<210> 20
 <211> 516
 <212> DNA
 <213> Homo Sapiens

<400> 20
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<210> 21
 <211> 482
 <212> DNA
 <213> Homo Sapiens

<400> 21
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 agaaatctaa tcagaaaact gacttttctc atgttcaact ggacctaggg gaatatgaca 180

8

gaaaagcacc ccataggcct taatatactt tttaaaatat ataaaactga aaattaatag 240
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atcacggaaa acaaatttat aaaagaaata actatatgcg cagtaattct taacacattg 480
ac 482

<210> 22
<211> 459
<212> DNA
<213> Homo Sapiens

<400> 22
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acttcggcag cggagccatg ttgcatgatg tggctcctggg tgtgcccga aacgctctgc 120
agcccactca cccagtgtac aacattggac cagacaaggt gatccaggcc actacatact 180
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aaggtttata cgtttcaata catactgcat totgtgctac acaagcctta gcctcagtgg 360
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<210> 23
<211> 549
<212> DNA
<213> Homo Sapiens

<400> 23
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agctgagta 549

<210> 24
<211> 372
<212> DNA
<213> Homo Sapiens

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tcacagcaaa aattcatgtt ttgtcagctt tctcatgttg agatctgtta tgtcactgat 180
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 agtgtttgtg tg 372

<210> 25
 <211> 475
 <212> DNA
 <213> Homo Sapiens

<400> 25
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 gctctgttgg tgtgcgtgtt ccgtggcgga gagaagaaaa tgggaaagac atctcactgg 420
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<210> 26
 <211> 516
 <212> DNA
 <213> Homo Sapiens

<400> 26
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 gtatacctca tttttcatac tgaaaaaaa agcttgtggc caatggaaca gtaagaacat 180
 cataaaattt ttatatatat agtttatttt tgtgggagat aaattttata ggactgttct 240
 ttgctgttgt tggtcgcagc taaataagac tggacattta acttttctac catttctgca 300
 agttaggtat gtttgccagg agaaaagtat caagacgttt aactgcagtt gactttctcc 360
 ctgttctctt gagtgtcttc taactttatt ctttgttctt tatgtagaat tgcgtgtctat 420
 gattgtactt tgaatcgctt gacttgttga aaatatttct ctagtgtatt atcactgtct 480
 gttctgcaca ataaacataa cagcctctgt gatccc 516

<210> 27
 <211> 566
 <212> DNA
 <213> Homo Sapiens

<400> 27
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 taagcggtea tcgttgcgtc atggggcagg cgtggggagc ttctgtcgc cttggctggg 120
 tgtgggcctg gaggaaggtc ctggggcgtg cactcgcctg ggcagtgggg aggagagtgg 180

10

cctgagttac ttcaaccccg cgtgctgctg gttaatgtcc cgcgtctctg caccttcggg 240
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cccagtaggt tcccagggtc cagcgtgccc ctccctcaga cacacggaca caatcagccg 360
agaagttcct ggtctgaatc acgagaatgt ggaggggtgg ggggtgtcag tggaaaggca 420
taaggctgag ctgagaccag ttgctggtga aactgggcca atctggggag gggaacatcc 480
ttgccaggga gtttctgagg gtctgctttg tttaccttcc gtgcgggtgga ttctttttaa 540
ctccgtctac ctggcgtttt gttaga 566

<210> 28
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<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (199)..(199)
<223> n is a, c, g, or t

<400> 28
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ctgagtccgc ctctgcang ggccagcccg ccagccctc tgcccacatg gtcagccaca 240
gtcactcccc ctctgtggtc tcctgaaggg agcgcctcct ccaacaacac gtggatctgc 300
atgggtttgcc tgagctttga acagtca 327

<210> 29
<211> 347
<212> DNA
<213> Homo Sapiens

<220>
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<223> n is a, c, g, or t

<400> 29
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tccagttagt gacttttgcc ccatagttgg ggtaancact tcctagattg agaaaaagca 180
gtacagtca atcctgctct gtttgctca tttggtgatc agtcagtcac acataagttc 240
cttgtattct aaatttcatt cacttctccc agatgctata ggggtttctc tcaactgttc 300
caatggatgt catccagaca gtgggctcat atcttacggg tttgtgc 347

<210> 30
<211> 210
<212> DNA
<213> Homo Sapiens

<400> 30
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11

acatgaatga acgtccagat gtttgtgcag tagccacccc ttatctgcag gatacgttcc 120
 aagaccccca gtgaatgcct gaaactgcag atagtactga atoctatata tactgtgttt 180
 tttatgatac atacatgcct atgatgaagt 210

<210> 31
 <211> 511
 <212> DNA
 <213> Homo Sapiens

<400> 31
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 ctgtgtgccca ggggctggtg ggacagtggg gacatagtct ctgccctcat agagttgatt 180
 gtctagttag gaagacaagc atttttaaaa aataaattta aacttacaaa ctttgtttgt 240
 cacaagtggg gtttattgca ataaccgctt ggtttgcaac ctctttgctc aacagaacat 300
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 ttgtgcacat ttctttgcat tccagctgtc actctgtgcc tttctacaac tgattgcaac 420
 agactgttga gttatgataa caccagtggg aattgctgga ggaaccagag gcacttccac 480
 cttggctggg aagactatgg tgctgccttg c 511

<210> 32
 <211> 505
 <212> DNA
 <213> Homo Sapiens

<400> 32
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 ttcagctgcc agtgtgttac tcatctttat cctaaaaatc tgggaatcaga gatttttgtt 180
 tggtcacata tgattctctt agacactttt atatttgaaa aaattaaaat ctttctttgg 240
 ggaaaaattc ttggttattc tgccataaca gattatgtat taactttag attcagtggg 300
 tcaatactg tttagttgct tgctaattt tccagaagga tttcttgat tggtgaaaga 360
 cggttgggga tggggggatt tttttgttct tggtgtacct ttgttttgaa actagaaatc 420
 tgtcctgtgg catgcaaaag aaagcaaatt atttttaaaa gaaaaaaacc aaagtacttt 480
 tgggtgcatt attccatctt ctcca 505

<210> 33
 <211> 307
 <212> DNA
 <213> Homo Sapiens

<400> 33
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 ttcttctctt gcttgtcaca gagcactaca ggatgcattc agtgggcttt tctggcagcc 180
 cagttaacca tttataagat ttggacctg gagctgaacc agggagctag caaaagtaaa 240

12

gcagacttat aaaattatag ctatgtgcag ctgcacaaca cagtccttcc actagcagct 300
gtgttaa 307

<210> 34
<211> 519
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (130)..(130)
<223> n is a, c, g, or t

<220>
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<222> (144)..(144)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (167)..(167)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (169)..(169)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (268)..(268)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (349)..(349)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (358)..(358)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (478)..(478)
<223> n is a, c, g, or t

<400> 34
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ccggcccgan ctccgtctat aaanagagca gccagttgca gggctenant ctgctttcca 180
actgcctgac tgcttgttcg tctcactggt gtgagctcca gcatccccctt tgctcgaaat 240
ggaccccaac tgctcttgcg ccaactgntg gctcctgcac gtgcgccggc tcctgcaagt 300
gcaaagagtg caaatgcacc tcctgcaaga agagctgctg ttctgtctnc cccgtggnct 360
gtgccaagtg tgcccagggc tgcgtctgca aaggggcacg ggagaagtgc agctgctgtg 420
cctgatgtgg gaacagctct tctccagat gtaaatagaa caacctgcac aacctggnat 480
ttttttaaaa atacaacact gagccatttg ctgcatttc 519

<210> 35

13

<211> 460
 <212> DNA
 <213> Homo Sapiens

<400> 35
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 taagggtgaaa aggggtgtgg caaaggagcc tactccaaga atggaggctg taggaatata 120
 acctcccacc ctgcaaaggg aatctcttgc ctgtccatc tcataggcta agtcagctga 180
 atcccgatag tactagggtcc ccttccctcc gcatcccgtc agctggaaaa ggctgtgtgc 240
 ccagaggctt ctccaaaggg agggtgacat gctggctttt gtgccaagc tcaccagccc 300
 tggccacact cactgcagta gtgcaccatc tcaactgcagt agcacgccct cctgggccgt 360
 ctggcctgtg gctaattggag gtgacggcac tcccatgtgc tgactcccc catccctgcc 420
 acgctgtggc cctgcctggc tagtcctgc ctgaataaag 460

<210> 36
 <211> 540
 <212> DNA
 <213> Homo Sapiens

<400> 36
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 ttgattgcaa ctacaaaggt ggactcaaag caaagcacia tcatgccagc caacattcca 180
 gaattctgct gagaactcca agtctgtgag gggagagggt ttacaagcca gacaggcctg 240
 ggggactgca gtccccaagg agaccctgcc acatgctggc cctttgagtg agaatgctgc 300
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 tataagatga agcgtagtga attgtacagc tgttgtaata atgacctatt tctatataaa 480
 ataaaattgt atggcttatg tgtaaattat tttgtatctg agataccagt tccttttccc 540

<210> 37
 <211> 367
 <212> DNA
 <213> Homo Sapiens

<400> 37
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 gtttgcaatg ctggtagaga tcacagagcg agccatggca cattgtggct ccaggaggc 180
 cctcattgtg ggaggagtgg ggtgtaatgt gaggctacag gagatgatgg caacaatgtg 240
 ccaggaacgt ggagcccggc tttttgctac agatgagaga ttctgtattg acaatggagc 300
 gatgatagcc caggctggct gggagatgtt tcgggctgga cacaggacc cactcagtga 360
 ttctggg 367

<210> 38
 <211> 532
 <212> DNA
 <213> Homo Sapiens

<400> 38
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 agtccttcac cttgccaggt gccgtttctc ttccgtgaag gccactgcc aggtccccag 120
 tgcgccccct agtggccata gcctggttaa agttccccag tgctccttg tgcataagacc 180
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 gccagtagtg tagtgccgtg tgcttttacg tgatggcggg tgggcagcgg gcggcgggct 360
 ccgcgcagcc gtctgtcctt gatctgccg cggcgcccg tgtgtgttt tgtgtgtgt 420
 ccacgcgcta aggcgacccc ctccccgta ctgacttct ctataagcg ttctcttcgc 480
 atagtacagt agtcccacc ccacctctt cctgtgtct acgcaagttt ta 532

<210> 39
 <211> 551
 <212> DNA
 <213> Homo Sapiens

<400> 39
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 tctgccccg ggtccccggc catccagcgg ggctgccaga gaacccaga cctgccctta 240
 cagtagtgta gcgccccct cctctttcgg ctgggtgtaga atagccagta gtgtagtgcg 300
 gtgtgtcttt acgtgatggc ggggtggcag cgggcggcgg gctccgcgca gccgtctgtc 360
 cttgatctgc ccgcgccggc ccgtgttgtg ttttgtgtg tgtccacgcg ctaaggcgac 420
 cccctcccc gtactgactt ctctataag cgcttctct cgcatagtca cgtagctccc 480
 accccacct ctctctgtgt ctacgcgaag ttttatact taatatttat atggcttttt 540
 ttcttcgaca a 551

<210> 40
 <211> 538
 <212> DNA
 <213> Homo Sapiens

<400> 40
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 gctcgaagca ggtttaggac caggtccct tgagaggtca gaggggcctc tgtgggtgct 120
 gggtagctca gaggtgccac tgggtgaagg gtcagcggag cccagtgcc tccttgtgca 180
 tagaccttot tctccaccc ccttctgccc ctgggtcccc ggccatccag cggggctgcc 240
 agagaacccc agacctgcc ttacagtagt gtagcgcctc ctccctctt cggtggtgt 300
 agaatagcca gtagttagt gcggtgtgct tttacgtgat ggcggtggg cagcgggcgg 360
 cgggtccgc gcagcgtct gtccttgatc tgcccgggc ggccgtgtt gtgttttgtg 420
 ctgtgtccac gcgctaaggc gacccctcc cccgtactga cttctctat aagcgcttct 480
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15

<210> 41
 <211> 403
 <212> DNA
 <213> Homo Sapiens

<400> 41
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 ccatccggaa cagggccttc tacatggagg agggcgtgcc ctattgcgag cgagactatg 120
 agaagatggt tggcacgaaa tgccatggct gtgacttcaa gatcgacgct ggggaccgct 180
 tcctggaggc cctgggcttc agctggcatg acacctgctt cgtctgtgcg atatgtcaga 240
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 ccttctctca tgtgtgagcc ccttctgccc acagctgccg cgggtggcccc tagcctgagg 360
 ggccctggagt cgtggccctg catttctggg tagggctggc aat 403

<210> 42
 <211> 437
 <212> DNA
 <213> Homo Sapiens

<400> 42
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 agtaaacgga cagatccatt cagtttgagc tgaaacacct agtcattttg ttcaggatct 360
 gttgacaatg gagcaagtga aagactttgc tgctaattgt tatgaagctt ttagtacctc 420
 tcagcaactg gagaaat 437

<210> 43
 <211> 520
 <212> DNA
 <213> Homo Sapiens

<400> 43
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 cggattccgg catccacatc atcctccgca ctgagtgagg gtggggagcc caggcctggc 120
 ctcggggcag ggcagggcgg ctaggccggc cagctcccc ttgcccgcca gccagtggcc 180
 gaacccccca ctccctgcca ccgtcacaca gtatttattg ttcccacaat ggctgggagg 240
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<210> 44
 <211> 530

16

<212> DNA
<213> Homo Sapiens

<220>
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<222> (68)..(68)
<223> n is a, c, g, or t

<400> 44
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tactagaata ttcaaaatca atcatgaagg cagttactat tttgagtcta aaggttttct 180
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catttgaagt cattgctttt gctacatgat ttgtgtgtgt gaaggacata ccacgtttta 300
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gaggtttttc cttctgtata agcacctact gacaaaatgt agaggccatt caaccgtcaa 420
acaccatttg gttatatcgc agaggagacg gatgtgtaaa ttactgcatt gctttttttt 480
tcagtttgta taacctctaa tctccgtttg catgatacgc tttgttagaa 530

<210> 45
<211> 485
<212> DNA
<213> Homo Sapiens

<400> 45
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ggctctgggtg atcgatgtca gtcagtcagt agaacctacc cacctcaccg gcctggaggt 120
cttgttccgg gactgcagga atgtctcgca gtttttccag aaaggaggag tcaaggaagc 180
ccttagtgaa cgagaactct tcaatgctgt ttcaggctta aacatcacag cagataatga 240
agctgatttt ttagctgaga tagaagcttt ggagaaaatg aatgaagatc acgttcagaa 300
gaatggaagg aaagctgctt cttttttgaa agatgatgga gaccaccac tactatatga 360
tgaatagcac taataccac tgcttcagt ttaacacagc agtgattgtc agctgccaat 420
agcaaatgaa gttatgggtg acttgaaata ccaaacctg aggagtgggc aatggtgctt 480
ctgtg 485

<210> 46
<211> 351
<212> DNA
<213> Homo Sapiens

<400> 46
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cctcccaaag tgctaggatt acaggcataa gccactgagc ccagccctag ttcagtatct 120
tttatgtaaa ttataaacat ctgcaacatt atgtatcata tgcagatact tattgcattt 180
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aattgtcatt cacacacctt cttttctgct tcgtttttac atatgtcttt gcctattaaa 300
gatattatcc ctctgtttta tttttctctt cattcttgta ttgcctttta a 351

17

<210> 47
 <211> 521
 <212> DNA
 <213> Homo Sapiens

<400> 47
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 cagctcagaa gaggaattct cacctcccca aagtccagac cagaactcgg tctttctgct 180
 gcagggcaat atggggccacg ccaggagctc aaactattct ctcccgggct taacagcctc 240
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 cctcacctcc agtctggtgg acttggggtc ctaagtgggg agggactggg gcctcgaagg 360
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 atttttgcag cttgtttctg gagttgtttg cgcataaagg aatggtggac tttcacaaat 480
 atctttttta aaatcaaaac caacagcgat ctcaagctta a 521

<210> 48
 <211> 498
 <212> DNA
 <213> Homo Sapiens

<400> 48
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 ggtgtgaaaa catggagtcc gttttatagt gactaaagga gggctgaact ctgtattagt 180
 aatccaaggg tcattttttt cttaaaaaaa gaaaaaaagg ttccaaaaaa aacaaaaact 240
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 ttttctcagc atcagagcca gacaggattc agaataagga gagaatgaca tcgtgcggca 360
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 ttttcaggat gctgacagct gcaagcaaca ggcactgcca aattcagggg acagtgggtg 480
 ccagcttgga ggatggac 498

<210> 49
 <211> 331
 <212> DNA
 <213> Homo Sapiens

<400> 49
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 atatatgacc ctgtctgtgg gactgatgga aatacttata ccaatgaatg cgtgttatgt 240
 tttgaaggtc ggaaacgcca gacttctatc ctcatcctaaa aatctggggc ttgctgagaa 300
 ccaaggtttt gaaatcccat caggtcaccg c 331

<210> 50
 <211> 548

<212> DNA

<213> Homo Sapiens

<400> 50

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atTTaaagcc tgtctgtggT gacgatggcc aaacctacaa caatccttgc atgctctgtc      180
atgaaaacct gatacgccaa acaaatacac acatccgcag tacagggaag tgtgaggaga      240
gcagcacccc aggaaccacc gcagccagca tgcccccgtc tgacgaatga caggaagatt      300
gttgaaagcc atgagggaaa aaataaacc cagttctgaa tcacctacct tcaccatctg      360
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tgggaaatgga atcactgatt ttcagtcttt tccatttctt tcctctaga atctgtgac      480
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gtctgtcc                                           548

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<210> 51

<211> 526

<212> DNA

<213> Homo Sapiens

<400> 51

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gtccacattc ctgcaagcat tgattgagac atttgcaaa tctaaaatgt aagcaaagta      60
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ttccttttag gaaggatgtg gatctccaaa taaagattta gtgtttattt tgagctctgc      180
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caggccagaa ctatagtcac actcacacaa agggagaaat ttaaactcga accaagcaaa      360
aggettccag gaaatagcat ggaaaaacaa tgcttccagt ggccacttcc taaggaggaa      420
caaccccgtc tgatctcaga attggcacca cgtgagcttg ctaagtata atatctgttt      480
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<210> 52

<211> 476

<212> DNA

<213> Homo Sapiens

<400> 52

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agcgaagtta tggaatatcg tggaaaggat actagttgtg aaatggaaag agacaagtta      180
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caattttctg ttgccacctt tataccggaa gactctgttg tagaagaaaa gaaggctttg      300
gtgcacctta tgtgggagga ggaggggagc ggcattgctga tgctgagcgt acaggcagac      360
aagagcgtag cctgctgttg cctccatcac tatgaaatga cttatTTTtac ctgaaggacc      420
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<210> 53
 <211> 501
 <212> DNA
 <213> Homo Sapiens

<400> 53
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 ggcggaatgt gctgtgtggg gccataaacac ccacgagat cgtgtgatg acctcagagg 180
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 cctttgttgt ctgcaacgag tgtggaaacc gctggaagtt ctgctgacct ctctgtaga 420
 tgtgtgcgag ccttggggcc tccccggccc acgtcctcg ttgacacagc ttctctggag 480
 accctagaag gcggcatgtc c 501

<210> 54
 <211> 453
 <212> DNA
 <213> Homo Sapiens

<400> 54
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 aggcagcctt cgacatcttc gtgctgggag ctgaggatgg ctgcatcagc accaaggagc 120
 tgggcaaggc gatgaggatg ctgggccaga accccacccc tgaggagctg caggagatga 180
 tcgatgaggt ggacgaggac ggcagcgcca cgggtggactt tgatgagttc ctggtcatga 240
 tggttcggtg catgaaggac gacagcaaag ggaaatctga ggagctgtct gacctcttcc 300
 gcatgtttga caaaaatgct gatggctaca tcgacctgga tgagctgaag ataatgctgc 360
 aggctacagg cgagaccatc acggaggagc acatcgagga gctcatgaag gacggagaca 420
 agaacaacga cggccgcacg gactatgatg agt 453

<210> 55
 <211> 498
 <212> DNA
 <213> Homo Sapiens

<220>
 <221> misc_feature
 <222> (142)..(142)
 <223> n is a, c, g, or t

<400> 55
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 caagttcccc ggagagtcgg gntccctgt gggccctca ggcctatgtc tgtgaggaag 180
 gggccctgcc actctcccca agagggcctc catgtttcga ggtgcctcaa catggagcct 240
 tgccctggcct gggctagggg cactgtctga actcctgact gtcaggataa actccgtggg 300
 ggtacaggag ccagacaaa gcccaggcct gtcaagagac gcagagggcc cctgccaggg 360

20

ttggccccag ggaccctggg acgaggtgc agaagctctc cctccctact ccctgggagc 420
 cacgtgctgg ccatgtggcc agggacggca tgagcaggag gcggggacgt gggggccttc 480
 tggtttggtg tcaacagc 498

<210> 56
 <211> 544
 <212> DNA
 <213> Homo Sapiens

<400> 56
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 gctcttctac tgtaattggg tgtggaaaaa ctctggcttt atggtattcc attaggttct 180
 tttcatttaa agtagtctta aatcaaagt atccaatatt ttaaagccac aaagtagatt 240
 acataattag cagagatttt agtcagtaaa atgtagaaa tcaaactata agaaaattca 300
 agtcccttat tttgtgtctt gggatatgt cattatttta aattccacac tcccttattt 360
 aatcactttg gtaagtgcct ttgatgtttt gaaatgtata gtgggagatg agcaaagtga 420
 aatgtcatgt gccctgttcc ctagcttctc aattcctcat aaccattttt accagtgttg 480
 caaagtttag accttgtgt taatatcaga agtgtatttg tagccctccc atagtgaaca 540
 atga 544

<210> 57
 <211> 535
 <212> DNA
 <213> Homo Sapiens

<400> 57
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 ggagctcgag cggcagatcg agagcacaga gacttcttgc catggctgcc gtaagaattt 120
 ctccctgtcc aagatccggt cccacgtggc tacttgttcc aaataccaga attacatcat 180
 ggaaggtgtg aaggccacca ttaaggatgc atctcttcag ccaaggaatg tcccaaaccg 240
 ttacaccttt cctgtctctt actgtctga gaagaacttt gatcaggaag gacttgtgga 300
 aactgcaaa ttattccata gcacggatac caaatctgtg gtttgtccga tatgtgctc 360
 gatgccctgg ggagaccca actaccgcag cgccaacttc agagagcaca tccagcgccg 420
 gcaccggttt tcttatgaca cttttgtgga ttatgatgtt gatgaagagg acatgatgaa 480
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<210> 58
 <211> 479
 <212> DNA
 <213> Homo Sapiens

<400> 58
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 cagcagaaag agaaatggaa tgtgcacgga tacacattca ctgctcagta agaggctcaa 120
 gacatgactg atttgcattt taaagcaaga tgcgatgtcc agagttacag agaatgagta 180

21

gatgtgtctc atcgggttaat agctctatta tacctctaaa ggtggaattg tcagttttaga	240
ttcataaatg aaaaggtaaa tgagtaatca gaataaacca agtgataatc aaaccatgtc	300
aagattatta gtacagactc tagcctgtta attttcttag ttgatttctg aagctacctg	360
atttattcta ttaaattgta agcttgcaaa ctcaaaataa attggcagat ttacctctca	420
tgttttaatg tgtcaaatta gagagcaaag tataacaggt gccttcactt ttgagactt	479

<210> 59
 <211> 518
 <212> DNA
 <213> Homo Sapiens

<400> 59	
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gcctcctaga tgtaacattc ctgatcaagg tacaattctt taaaattcac taatgattga	120
ggtccatatt tagtggtact ctgaaattgg tcactttcct attacacgga gtgtgctaaa	180
actaaaaagc attttgaaac atacagaatg ttctattgtc attgggaaat ttttctttct	240
aaccacagtgg aggttagaaa gaagttatat tctggtagca aattaacttt acatcctttt	300
tctacttgt tatggttgtt tggaccgata agtgtgctta atcctgaggc aaagtagtga	360
atatgtttta tatgttatga agaaaagaat tgttgtaagt ttttgattct actcttatat	420
gctggactgc attcacacat ggcattgaaat aagtcagggt ctttacaat ggtattttga	480
tagatactgg attgtgtttg tgccatattt gtgccatt	518

<210> 60
 <211> 489
 <212> DNA
 <213> Homo Sapiens

<400> 60	
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aactttacaa atccatgaag ggtgctggca cagatgagaa gactctgacc aggatcatgg	120
tatcccgcag tgagattgac ctgctcaaca tccggaggga attcattgag aaatatgaca	180
agtctctcca ccaagccatt gagggtgaca cctccggaga cttcctgaag gccttgctgg	240
ctctctgtgg tggtaggac tagggccaca gctttggcgg gcacttctgc caagaaatgg	300
ttatcagcac cagccgccat ggccaagcct gattgttcca gctccagaga ctaaggaagg	360
ggcaggggtg gggggagggg ttgggttggg ctcttatctt catggagctt aggaaacgct	420
cccactccca cgggccatcg agggccagca cggctgagcg gtgaaaaacc gtagccatag	480
atcctgtcc	489

<210> 61
 <211> 472
 <212> DNA
 <213> Homo Sapiens

<400> 61	
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atgcaaatgt cagcaagaat atttcggtga acgggtgtgg gaaaagtcca tgaaaactca	120
cagcatgatt gacagtagtt tatcaaaaat tgcattagca gccatagctg cctttatgtc	180

22

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tgctgtgac ctcacagctg ttgctgttat tacagtccag cttagaagac aatacgtcag 240
gaaatatgaa ggagaagctg aggaacgaaa gaaacttcga caagagaatg gaaatgtaca 300
tgctatagca taactgaaga taaaattaca ggatatcaca ttggagtcac tgccaagtca 360
tagccataaa tgatgagtcg gtctctcttc cagtggatca taagacaatg gacccttttt 420
gttatgatgg ttttaaactt tcaattgtca ctttttatgc tatttctgta ta 472

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<210> 62
<211> 523
<212> DNA
<213> Homo Sapiens

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<220>
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<223> n is a, c, g, or t

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<220>
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<222> (440)..(440)
<223> n is a, c, g, or t

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<220>
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<223> n is a, c, g, or t

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<220>
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<223> n is a, c, g, or t

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<220>
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<223> n is a, c, g, or t

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<220>
<221> misc_feature
<222> (493)..(498)
<223> n is a, c, g, or t

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gaatggctct aagctggcaa gccgcattct gagcaaatta actgatatcc agtatggaag 180
agaagagagc gactggacaa ttgtgctatc ctgaatggaa aatagaggat acaatggaaa 240
atagaggata ccaactgtat gctactggga cagactgttg catttgaatt gtgatagatt 300
tctttggcta cotgtgcata atgtagtttg tagtatcaat gtgttacaag agtgattgtt 360
tcttcatgcc agagaaaatg aattgcaatc atcaaatggg gtttcataac ttggtagtag 420
taacttacct taccttaccn anaaaaatat taatgtaagc catataacat gggattttcc 480
tcaannannn nannnnnncc ttttgtactt cactcagata cta 523

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<210> 63
<211> 373
<212> DNA
<213> Homo Sapiens

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23

<400> 63
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 aactgtgaag atctgacttc gccccccccc ccccccattct tggggaccag gatttgcaca 120
 gaagcacatg cacctaccca tacaccccct cttctgagcg tccctgttcc cccatctcgc 180
 tccctcccag gactctgacc ccagcattct caggcaccag tccctgtccg gaatgccacc 240
 cacatcttcc atttccatgt cccctcccag agctggtgga cccagggaac agccactccc 300
 ctccactctc taccagataa ctgaggaggg gagaggtggg ccgtaacggg cacggatcac 360
 gatgtaaatt att 373

<210> 64
 <211> 535
 <212> DNA
 <213> Homo Sapiens

<400> 64
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 cccagctgct gattgtgctg ctgggcctca gcgctctgct gcagtgagat cccaggaagc 180
 tggcacatct tggaaggtcc gtccctgctcg gcttttcgct tgaacattcc cttgatctca 240
 tcagttctga gcggtcatg gggcaacacg gttagcgggg agagcacggg gtagccggag 300
 aagggcctct ggagcaggtc tggaggggcc atggggcagt cctgggtgtg gggacacagt 360
 cgggttgacc cagggtgtc tccctccaga gcctccctcc ggacaatgag tccccctct 420
 tgtctccac cctgagattg ggcattgggt gcggtgtggg gggcatgtgc tgctgttgt 480
 tatgggtttt ttttggggg ggggttgctt ttttctgggg tctttgagct ccaaa 535

<210> 65
 <211> 452
 <212> DNA
 <213> Homo Sapiens

<400> 65
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 cgccgcctc caggagctgc tggagtccaa ccggcagaca cgctggagt tccagcagca 120
 gctcggggag gccccagtg atgccagccc ctaggctcca agagcccca accgggaccc 180
 aacctgcct ccctgggcta ggctctggcc tgggcaactca cccctggct tagacacctt 240
 ctcaagggtt ggccttcagg gaccctggt gggctctgct gcctgggcca cccttctgc 300
 ctgggcctcc ccttggccta cctgggcccag cccccaccac ctggcatgcc ctctggggc 360
 caagagtggg cctgcaaccc accacttgc ctgcccaccc aactcctggg cgctccccc 420
 tctgccagg ccttgagtgt ccacattaaa tg 452

<210> 66
 <211> 323
 <212> DNA
 <213> Homo Sapiens

<400> 66
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24

ggttgtaaat tagaaaagct gggattacat atgggtgtgcg gttacagtct aaattttttc 120
 atcctcctat gcatcataag catgttttga atattttcaa aaatagttct actgatgcta 180
 caggaatttc aagcctgtgg tgaatgttag tattttaccat agggagtga gttggagtat 240
 ggtttcattc aatagagtat tgotgattat acttgagtgg aatcctttcc tcacgtactc 300
 ccacagacgt ctgggcctgg aaa 323

<210> 67
 <211> 560
 <212> DNA
 <213> Homo Sapiens

<400> 67
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 cgcagtgcaa ggcctgaacc tgaggagccc caacaacttc ctgtcctact accgcctcac 180
 acgcttcctc tccagagtga tcaagtgtga cccggactgc ctccgggcct gccaggagca 240
 gatcgaagcc ctgctggagt caagcctgcg ccaggcccag cagaacatgg accccaaggc 300
 cgccgaggag gaggaagagg aggaggagga ggtggacctg gcttgcacac ccaccgacgt 360
 gcgggacgtg gacatctgag ggcgccaggc aggcgggcgc caccgccacc cgcagcgagg 420
 gcggagccgg cccaggtgc tcccctgaca gtccctcctc tccggagcat tttgatacca 480
 gaagggaaag cttcattctc cttgttgttg gttgtttttt cctttgtctc tcccccttc 540
 catctctgac ttaagcaaaa 560

<210> 68
 <211> 471
 <212> DNA
 <213> Homo Sapiens

<400> 68
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 acaccataat gctaatttaa agagactcca aatctcaatg aagccagctc acagtgtgtt 120
 gtgccccggt catctagcaa gctgccgaac caaagaatt tgcacccgcg tcggggccca 180
 cgtgggttggg gccctgccct ggcagggtca tcctgtgtc gagggccatc tcgggcacag 240
 gccaccccg cccacccct ccagaacacg gtcacgctt acctcaacca tcctggctgc 300
 ggcgtctgtc tgaaccacgc gggggccttg agggacgctt tgtctgtcgt gatggggcaa 360
 gggcacaagt cctggatgtt gtgtgtatcg agaggccaaa ggctgggtggc aagtgcacgg 420
 ggcacagcgg agtctgtcct gtgacgcgca agtctgaggg tctggggcggc g 471

<210> 69
 <211> 518
 <212> DNA
 <213> Homo Sapiens

<400> 69
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 gctcttctgt tttcttcgga ggagagcggg ggtcaaagag cccttactgc cccagagga 120

25

tgacacccgg gacaacgttt attactatga tgaagaagga ggccggagaag aggaccagga	180
ctttgacttg agccagctgc acaggggcct ggacgctcgg cctgaagtga ctcgtaacga	240
cgttgaccca accctcatga gtgtcccccgt gtatcttccc cgccttgcca atccccgatga	300
aattggaaat tttattgatg aaaatctgaa agcggctgat actgacccca cagccccgcc	360
ttatgattct ctgctcgtgt ttgactatga aggaagcggg tccgaagctg ctagtctgag	420
ctccctgaac tcctcagagt cagacaaaga ccaggactat gactacttga acgaatgggg	480
caatccgttc aagaagctgg ctgacatgta cggaggcg	518

<210> 70
 <211> 182
 <212> DNA
 <213> Homo Sapiens

<400> 70	
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gggcattttct tgcgagcctc gcagcctccg gaagctgtcg acttcatgac aagcattttg	120
tgaactaggg aagctcaggg ggggttactgg cttctcttga gtcacactgc tagcaaattg	180
ca	182

<210> 71
 <211> 538
 <212> DNA
 <213> Homo Sapiens

<400> 71	
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agcgcgccgag tggcggagct gctgctgctc caaggcgcgg agcccaactg cgcgcacccc	120
gccactctca cctgaccctg gcacgacgct gcccgaggagg gcttctctgga cagcgtgggtg	180
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ggcaccagag gcagtaacca tgcccgcata gatgccacgg aaggtccttc agacatcccc	360
gattgaaaga accagagagg ctctgagaaa cctcgggaaa cttagatcat cagtcaccga	420
aggtcctaca gggccacaac tgcccccgcc acaaccacc ccgctttcgt agttttcatt	480
tagaaaatag agctttttaa aatgtcctgc cttttaacgt agatatatgc cttcccc	538

<210> 72
 <211> 513
 <212> DNA
 <213> Homo Sapiens

<400> 72	
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tcgtcaaatg tcaaatattc tctctttggc tggaatgaca aaaactcaaa taaatgtatg	120
attaggagga catcataacc tatgaatgat ggaagtccaa aatgatggta actgacagta	180
gtgttaatgc cttatgttta gtcaaaactct catttaggtg acagcctggg gactccagaa	240
tggagccagt catgctaaat gccatatact cacactgaaa catgaggaag caggtagatc	300
ccagaacaga caaaactttc ctaaaaaacat gagagtccag gctgtctgag tcagcacagt	360

26

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 ccaatcagtt tatttaaato aatttattta tattctcttg ttcctggatt cccattttac 480
 aaaaccact gtctactgt tgtattgccc agt 513

<210> 73
 <211> 530
 <212> DNA
 <213> Homo Sapiens

<400> 73
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 aggggaatat atgaattggt taacaaatta gaatttgttt acaactactt gaatttttaa 180
 attatgtcaa aacttacatt acttgccaag cagtatgatg ttataggaaa cataaataag 240
 attacagagg tatcaatttg gttaaaattc accattttat aagactaagc aataatctta 300
 acaacctctt tcctgaatat ttaaatgtgt ttgtatggtg ttatgactaa ttgttactga 360
 tttagagact aagccctctt aaaaccttta gttaaatata aaaagaaatt atatatatct 420
 tgctccctg atggaaaact atataaaatt gtagacttaa aaggtttgtg gaaatacatt 480
 aggatatcag aaaactaaat atatggagtt gctttatgac tattacatgt 530

<210> 74
 <211> 406
 <212> DNA
 <213> Homo Sapiens

<400> 74
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 aacctcacgc aaggcgaaga ccagtactat ctgcgggtca ccacggtggc ttcccacact 300
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 cccatcactg tgacggtccc tgtagaagtc tccaggaaga acccta 406

<210> 75
 <211> 286
 <212> DNA
 <213> Homo Sapiens

<400> 75
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 accagtacta tctgcgggtc accacggtgg cttccacac ttctgactcg gacgttcctt 120
 ccggtgtcac tgagggtgtc gtgaagctct ttgactctga tccatcact gtgacggtcc 180
 ctgtagaagt ctccaggaag aacctaaat ttatggagac cgtggcggag aaagcgctgc 240
 aggaataccg caaaaagcac cgggaggagt gagatgtgga tgttgc 286

<210> 76

27

<211> 436
 <212> DNA
 <213> Homo Sapiens

<400> 76
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 tccgttttca ttgttcactt ctaaacaaaa aattatgtgt tgccaaaacc aaaccaggt 120
 tcatgaatat ggtgtctatt atagtgaac atgtactttg agcttattgt ttttattctg 180
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 caacaacctt aaaggccgtc atttcattag tattcctcat totgcatcct ggcttgaaaa 300
 acagctctgt tgaatcacag tatcagtatt ttcacacgta agcacattcg ggccatttcc 360
 gtgggtttctc atgagctgtg ttcacagacc tcagcagggc atcgcatgga ccgcaggagg 420
 gcagattcgg accact 436

<210> 77
 <211> 429
 <212> DNA
 <213> Homo Sapiens

<400> 77
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 cgtcccccgg ctctgcctg gaggagttaa gaagtgcgcc attcatcgag tgtcacggcc 120
 gtgggacctg caattactac gcaaacgctt acagcttttg gctcgccacc atagagagga 180
 gcgagatgtt caagaagcct acgccgtcca ccttgaaggc aggggagctg cgcacgcacg 240
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 aacatggtgc tacttcttct tctttttgtt aacagcaacg aaccctagaa atatctctg 360
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 acaccctgc 429

<210> 78
 <211> 195
 <212> DNA
 <213> Homo Sapiens

<400> 78
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 gatccatcca tctccaggga gcaagacaga gacgcaggat ggaaagcggg gttcctaaca 120
 ggatgaaagt tccccatca gttccccag tacttccaag caagtagctt tcacatttg 180
 tcacagaaat cagag 195

<210> 79
 <211> 301
 <212> DNA
 <213> Homo Sapiens

<400> 79
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 gcaatgtcac aacctctctg atcttgtgct cagcatgatt cttaataaga agttttattt 120
 ttcgtgcact ctgctaata tgtgggtgag ccagtggaac agcgggagcc tgtgctggtt 180

28

tgcagattgc ctcctaataga cgcgggtcaa aaggaaacca agtgggtcagg agttgtttct 240
gacccactga tctctactac cacaaggaaa atagttagg agaaaccagc ttttactgtt 300
t 301

<210> 80
<211> 459
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (164)..(164)
<223> n is a, c, g, or t

<400> 80
ggaaacgttc ccagttcatt ttcagtcctg ttgtgagcac agttctgaag ggtttattat 60
tgtcaaaata agttttgttt tgttttgttt atgttgggtt tttaatgttg tctcttgacc 120
cttaatgttc aggttcttctg gggaggttaat cagccacatc caangttacc ttgaggggga 180
agaagagggt gatgctcaga agctaaacaa gacaggggcc acatgaccct ctattgatta 240
gccccaaagta gaaagtctctg tgggttttatg tttaatggta atagttagtc atatatggca 300
taattttcta tcagcttcct actcagtcac tataaacaca gacttgaaat agtactttaa 360
atgtccaaat acctaaatgt gctaaactgg aggtaactat ttctaggtag ttgaattttt 420
gaaagtcattg atcagccaca caactgtttt gtacataact 459

<210> 81
<211> 394
<212> DNA
<213> Homo Sapiens

<400> 81
aatccttatt gttcagagtt gtttgggggt totgtttcag agcataaaac ctaaaggtta 60
tagtagaaca aggcaccttc ttaaaagaaa tottgcttca gaccatcagt tacagagaat 120
ttcctaaagt aaaattgaag caactacaac ttctccttag acactttgga atctaaccac 180
ttaaggacct ttttaaagag atagcttctc ttctttctga agatcaattt ctccaaggc 240
caagattgtc cttttctccc atttcttgct agctattgca aatgagggaa gaacattatt 300
catctctcct cccctttttt ttctgattct ttttccagtc agttttgctc ctgggttcaa 360
gtagtattac caccctttca caagcaacag actc 394

<210> 82
<211> 514
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (89)..(89)
<223> n is a, c, g, or t

<400> 82
gctcactaca ctattcattg cacacaaatg aatttttcac tttttaagat gcattcttgg 60
tgctcaaacc agatogaagt ttgtctctna aagctattgt ctgcacaggc tgctgcatgc 120

29

tctgttggtta aatggatgga caggctattc taaattttgg ttgatacttt tgctactatg 180
ggcaattaac ttgaaaaaaa taatcgatcc caactctgtg ctctgatgta cctcttctgc 240
cccttttatg acacctttga ccaaatgcct tctatgggtc acagtgcagg cacaaaacta 300
cctctgatac agaaggttct ttacaagctt attttacata ccgatgaatcc ctcacctaaa 360
gggagagggtg aaagcaaaga ctgctttgaa tgggtattga gggagattgt gtccatacca 420
agccaccctg aagaagtatt tcaactgcag tagaactgtg gattttgtgct gtcatttcac 480
cttggaataa acacctatct ctaagcagga ccaa 514

<210> 83
<211> 299
<212> DNA
<213> Homo Sapiens

<400> 83
caccaaatta cctaggctga ggtagagag attggccagc aaaaactgtg ggaagatgaa 60
ctttgtcatt atgatttcat tatcacatga ttatagaagg ctgtcttagt gcaaaaaaca 120
tacttacatt tcagacatat ccaaaggga tctcacatt ttgttaagaa gttgaactat 180
gactggagta aaccatgtat tcccttatct tttacttttt ttctgtgaca tttatgtctc 240
atgtaatttg cattactctg gtggattggt ctagtactgt attgggcttc ttcgtaaat 299

<210> 84
<211> 219
<212> DNA
<213> Homo Sapiens

<400> 84
ttatcgccct gagaagatct accccagga gaatctgaga catcttgcc acttttcttt 60
attagcttct tctcatcca tttcttttat acctttcctt tttggggagt tgttatgcc 120
tgatttttgg tatttatgta aaaggattat tactaattct atttctctat gtttattcta 180
gttaaggaaa tgttgagggc aagccaccaa attacctag 219

<210> 85
<211> 518
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (61)..(65)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (71)..(71)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (73)..(73)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (112)..(112)

<223> n is a, c, g, or t

<220>

<221> misc_feature

<222> (163)..(163)

<223> n is a, c, g, or t

<220>

<221> misc_feature

<222> (295)..(295)

<223> n is a, c, g, or t

<400> 85

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aaggactggt atctttctgt gagcaataag gactggataa agactgcata tccttggtgc 60
nnnnncagca ncnatacaat aaggagggtt ttaatgtgaa gcaggcaatc tncagcccc 120
ttctggtctt ggatgaaata gttgcacaga gtattgcacc aanaatacac aatggagggt 180
gaaaagtcca acatatttta agtcaattaa tcaaattgca ttgattcttg atgctttctt 240
agaggcctac atgatttctt agattgctct gataaactat cataaggggt ccacntcccc 300
tcatttagct ccccaggga tttcttttcc cccatgtcat acaccagtc ctaaatcaac 360
ccccaaggct atccttccat cccttctgca gagggaaactt ttgtcagact ctgcaacaaa 420
ctcctagctc tatccagagt gtcctctgct gctaagattg gtatctttct cctcaaaagc 480
ctggatgggtg aatgggggtg cattagtcag aattctcc 518

```

<210> 86

<211> 458

<212> DNA

<213> Homo Sapiens

<400> 86

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taaaaacctg tatctgaccc actttgtaat ttttgctcca atatccattc tgtagacttt 60
tgaaaaaaaa gtttttaatt tgatgccccaa tatattctga ccgttaaaaa attcttggtc 120
atatgggaga agggggagta atgacttgta caaacagtat ttctggtgta tattttaatg 180
tttttaaaaa gagtaatttc atttaaatat ctgttattca aatttgatga tgttaaatgt 240
aatataatgt attttctttt tattttgcac tctgtaattg cactttttta gtttgaagag 300
ccattttggt aaacggtttt tattaagat gctatggaac ataaagttgt attgcatgca 360
atttaaagta acttatttga ctatgaatat tatcgatta ctgaattgta tcaatttggt 420
tgtgttcaat atcagctttg ataattgtgt accttaag 458

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<210> 87

<211> 336

<212> DNA

<213> Homo Sapiens

<400> 87

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gggatcctat ttagctctta gtaccactaa tcaaaagttc ggcattgtagc tcatgatcta 60
tgctgtttct atgtcgtgga agcaccggat gggggtagtg agcaaatctg ccctgctcag 120
cagtcacat agcagctgac tgaaaatcag cactgcctga gtagttttga tcagttaaac 180
ttgaatcact aactgactga aaattgaatg ggcaaataag tgcttttgc tccagagtat 240
gcgggagacc cttccacctc aagatggata tttcttcccc aaggatttca agatgaattg 300
aaatttttaa tcaagatagt gtgctttatt ctgttg 336

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31

<210> 88
 <211> 521
 <212> DNA
 <213> Homo Sapiens

<400> 88
 atatcttctt caggctctga caggcctcct ggaaacttcc acatattttt caactgcagt 60
 ataaagtcag aaaataaagt taacataact ttcactaaca cacacatatg tagatttcac 120
 aaaatccacc tataattggt caaagtgggt gagaatatat tttttagtaa ttgcatgcaa 180
 aatttttcta gcttccatcc tttctcctc gtttcttctt tttttggggg agctggtaac 240
 tgatgaaatc ttttccacc ttttctcttc aggaaatata agtggttttg tttggttaac 300
 gtgatacatt ctgtatgaat gaaacattgg agggaaacat ctactgaatt tctgtaattt 360
 aaaatatttt gctgctagtt aactatgaac agatagaaga atcttacaga tgctgctata 420
 aataagtaga aaatataaat ttcataacta aaatatgcta ttttaaaatc tatttcctat 480
 attgtatttc taatcagatg tattactctt attatttota t 521

<210> 89
 <211> 503
 <212> DNA
 <213> Homo Sapiens

<400> 89
 gtggctatcc actgttagtt cagaagctgg gcttggaacta ctcttatgat ttagctccac 60
 gagccaaaat tttccggcgt gaccaaggga aagtgactga tacggcatcc atgaaatata 120
 tcatgcgata caacaattat aagaaggatc cttacagtag aggtgacccc tgtaatacca 180
 tctgctgccg tgaggacctg aactcaccta acccaagtcc tggaggttgt tatgacacaa 240
 aggtggcaga tatctaccta gcatctcagt acacatccta tgccataagt ggtccacag 300
 tacaaggtgg cctccctgtt tttcgtggg accgtttcaa caaaactcta catcaggga 360
 tgccagaggt ctacaacttt gattttatta ccatgaaacc aattttgaaa cttgatataa 420
 aatgaaggag ggagatgacg gactagaaga ctgtaataa gataccaaag gcactatttt 480
 agctatgttt ttcccatcag aat 503

<210> 90
 <211> 275
 <212> DNA
 <213> Homo Sapiens

<400> 90
 ccccatcacg gaggggtccag actgtccact cgggggtgga gtgagactga ctgcaagccc 60
 caccctcctt gagactggag ctgagcgtct gcatacgaga gacttggttg aaacttggtt 120
 ggtccttgtc tgcaccctcg acaagaccac actttgggac ttgggagctg gggctgaagt 180
 tgctctgtac ccatgaactc ccagtttgcg aattaataag agacaatcta ttttggttact 240
 tgcacttggt attcgaacca ctgagagcga gatgg 275

<210> 91
 <211> 405
 <212> DNA

32

<213> Homo Sapiens

<400> 91

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tcattctgatg tttctatagt cactttgcc gctcaaaaga aaacaatacc ctatgtagtt      60
gtggaagttt atgctaatat tgtgtaactg atattaaacc taaatgttct gcctaccctg      120
ttggtataaa gataatttga gcagactgta aacaagaaaa aaaaaatcat gcattcttag      180
caaaattgcc tagtatgtta atttgctcaa aatacaatgt ttgattttat gcactttgtc      240
gctattaaca tccttttttt catgtagatt tcaataattg agtaatttta gaagcattat      300
tttaggaata tatagttgtc acagtaaata tcttgttttt tctatgtaca ttgtacaaat      360
ttttcattcc ttttgctctt tgtggttggg tctaactacta actgt                      405

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<210> 92

<211> 375

<212> DNA

<213> Homo Sapiens

<400> 92

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aagctatgtg tatcttctgt gtaaagcagt ggcttccactg gaaaaatggt gtggctagca      60
tttccctttg agtcatgatg acagatgggtg tgaaaacccat ctaagtttgc ttttgaccat      120
cacctcccag tagcaatttg ctttcataat ccatttagca atccaggcct ctggtgaaaa      180
gataatatga gggagaaggg aacacatttc cttctgaact tacttccta agtcactttc      240
cttatgtatc atctaataca atgatgggtg agtgaaaata cagaaggggt gtttgagtat      300
tcagatttca taaaacactt ccttggaata tagctgcatt aacttggaag gaagcctggt      360
gggccagaag acaga                      375

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<210> 93

<211> 533

<212> DNA

<213> Homo Sapiens

<400> 93

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gctggtgtgt gtgtcaaacc ctactcacc cagcactca cacacagcat tctgttctcc      60
atgcaaagtt aagatcgaat ccatccgctt gtaggggaaa aaaaggaaaa aaattaacca      120
gagagggtct gtaatctcgc agagcacagg cagaatcggt ccttccttgc tgcatttcct      180
ccttagacta atagacgttt tggaaagtcc ggctagtgtt cgtgtgtttg tcgtagcacc      240
cagagcctcc accaaaccct ctccatgtct ttacctcca gtcgctctaa gatctgcttg      300
aagtctcgta tttgtactgc tttctgcttt tctccacccc ctctagcac ccccatatcc      360
cccatctagt aacatctcag aaatttcctc cagaggaaca aaaaaattaa aaatagaaca      420
tagcaaagca aagacagaat gccccccccc aaatattgtc ctgtccctgt ctgggagttg      480
tgttatttaa agatattctg tatgttgtat cttttgcatg tagcttcctt aat          533

```

<210> 94

<211> 413

<212> DNA

<213> Homo Sapiens

<400> 94

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atctggaagg ctctgatcca cctgagcgac ctccgggagt acaggcgctt tgagaaggag      60

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33

aagctcaagt cccagtggaa caatgataat ccccttttca agagcgccac cacgacggtc 120
 atgaacccca agtttgctga gagttaggag cacttggtga agacaaggcc gtcaggaccc 180
 accatgtctg ccccatcacg cggccgagac atggcttggc cacagctctt gaggatgtca 240
 ccaattaacc agaaatccag ttatttttccg ccctcaaat gacagccatg gccggccgggt 300
 gcttctgggg gctcgctggg gggacagctc cactctgact ggcacagtct ttgcatggag 360
 acttgaggag ggcttgaggt tggtagggtt aggtgctgtt ttctgtgca agt 413

<210> 95
 <211> 465
 <212> DNA
 <213> Homo Sapiens

<400> 95
 cagcccgcc agttggagtt gtagtaccac gagggacgcc aactcccaga ggagtcctgt 60
 ccacccgagg gccagtgagt cggggaagag gacttctcac tcccagagca agaggagtcc 120
 cccaactgg gtacagacct ccaccgccac ccccgacaca agagacttat ggagaatatg 180
 actatgatga tggatatggc actgcttatg atgaacagag ttatgattcc tatgataaca 240
 gctatagcac ccagcccaa agtgggtgctg attactatga ttacggacat ggactcagtg 300
 aggagactta tgattctac gggcaagaag agtggactaa ctcaagacac aaggcacctt 360
 cagcgaggac agcaaagggc gtctacagag accagccata tggcagatac tgattgtact 420
 gtctgatgtt gtgaaatagc caatctccac cagtcctgta tactg 465

<210> 96
 <211> 537
 <212> DNA
 <213> Homo Sapiens

<400> 96
 gagaacacgg tggcagagac ggagtgccgc tatgccctgc agctgcagca gatccagga 60
 ctcatcagca gcatcgaggc ccagctgagc gagctccgca gtgagatgga gtgccagaac 120
 caagagtaca agatgctgct ggacatcaag acacgtctgg agcaggagat cgccacctac 180
 cgcagcctgc tcgaggcca ggacgccaag aagcgtcagc ccccgtagca cctctgttac 240
 cacgacttct agtgcctctg ttaccaccac ctctaagtc tctggctgcc gcacttctga 300
 tgtccgtagg ccttaaactc gcctggcgct cctccctct gtcttcagca ccagaggag 360
 gagagagccg gcagttccct gcaggagaga ggaggggctg ctggacccaa ggtcagtc 420
 ctctgctctc aggacccctc gtctgactc tctctgatg gtgggccctc tgtctcttc 480
 tcttcggctc ggatctctct cctctctgac ctggatacgc tttggtttct caacttc 537

<210> 97
 <211> 372
 <212> DNA
 <213> Homo Sapiens

<400> 97
 aactttaact tagagcttca ttactttaag aatggaaaac aacctctgag tttgatttcc 60
 caaagtttca taaagccctc aagctcatga ttttcatcaa ctctttgcc acatagtcac 120
 ttacctccac agccgtttgt tgtcatagaa ggggtggtgg tgtttggatt tgattttttt 180

34

caacttgacg tgagaaatag gataggtgac aaaaccttac ttgttttctt aagacaattc 240
 agtgcttgag catctctgtc agaaatggaa tgaaatactg ttagccaatt agaattatct 300
 tatgtattgt tattgtgttt tgctgatttt tatatgaaaa tataattatt cattcttgat 360
 ctctggaagc aa 372

<210> 98
 <211> 365
 <212> DNA
 <213> Homo Sapiens

<400> 98
 gggagccaag gctttatacg tctaaagaaa atattcagta gctgaatccg cccagtgata 60
 gcctgtgggc accagcagca agggctgcc a tgggatacag caccatcta caaagacctc 120
 tattacataa acaactgcttc ttacaggaaa caaacctctt ctgggatctc cttttgtgaa 180
 aaccagtttg atgtgctaaa agtaaaaagt ctattttcca gtgtggtctt gttcagaagc 240
 agccagattt ccaatgttgt ttttccctc cactcagaaa ccctgccct ttccttcag 300
 aaaacgatgg caggcattcc tctgagtta caagcagaga ctactcaa cccaaactag 360
 ctggg 365

<210> 99
 <211> 465
 <212> DNA
 <213> Homo Sapiens

<220>
 <221> misc_feature
 <222> (110)..(110)
 <223> n is a, c, g, or t

<400> 99
 acacacacat gcaattttgc ttaacaaaag tattttataa tacagtttca tacagaatta 60
 ccttaaaagg gagtcttatg ttttcaacta cagatagttg taagggatcn tacagaagat 120
 attgatgata gttgaaatat tcttagaagg ggtgtgtatg tctagctgtg tctaccatgt 180
 gtatgtatc ttgacaagca gtataaaata cctgtgattt ttctttacat tagggataat 240
 gcataaggaa ttaatcttca tatatattat catcccta gtagcagggg gaagtattta 300
 attgcccatg atatgtattt tacttatact atgccagaga ggaaactata aagtaattac 360
 acatgtaatc ttgggttttt cacatatgta ggtattcatt ttgagtaggt tgaagaagaa 420
 aaaaaatatt taaatgaatt gaattcctga tgggatagta tcaat 465

<210> 100
 <211> 515
 <212> DNA
 <213> Homo Sapiens

<400> 100
 gaactctgca tcttcatggt ttacagaaat tgggtgcaggc agccagcagt tagattccat 60
 tcatgtaaca cagttggaga gagataccgt ttagtggtgt ttagacaaat ttgtgaaaat 120
 tgtaaactca caaggaaaat taaaatcaag taagaaactg gcctctgagt taagttttga 180

35

ttttcgcatt gaatctgtag tatgccttca agacagtgtg ttggctttct ggaaacatgg	240
gatgcagggt aaaagcttca agtcagatga ggttaccag gagatttcag atgaaacaag	300
agttttccgc ttattaggat cagacagggt tgcgttttg gaaagtaggc caacagaaaa	360
tcctactgca cacagcaatc tctacatctt ggctggacat gaaaatagtt actaagcaac	420
agaaactgat ctcaaatgac aggaaaatga atatactoca ttgaaaggga aaataaggaa	480
attcaataca aactgcacta tgatttgctt taact	515

<210> 101
 <211> 525
 <212> DNA
 <213> Homo Sapiens

<400> 101 ctcagagcca cccctaaaga gatcctttga tattttcaac gcagccctgc tttgggctgc	60
cctgggtgctg ccacacttca ggctcttctc ctttcacaac cttctgtggc tcacagaacc	120
cttggagcca atggagactg tctcaagagg gcactgggtg cccgacagcc tggcacaggg	180
cagtgggaca gggcatggcc aggtggccac tcagacccc tggcttttca ctgctggctg	240
ccttagaacc tttcttacct tagcagtttg ctttgtatgc actttgtttt tttctttggg	300
tcttgttttt tttttccact tagaaattgc atttctgac agaaggactc aggttgtctg	360
aagtcactgc acagtgcac tcagcccaca tagtgatggg tcccctgttc actctactta	420
gcattgtccct accgagtctc ttctccactg gatggaggaa aaccaagccg tggcttcccg	480
ctcagccctc cctgcccctc ccttcaacca ttcccatgg gaaat	525

<210> 102
 <211> 418
 <212> DNA
 <213> Homo Sapiens

<400> 102 gcaacaaccg aaaaatgcacc agccccaggt cctcgacac cgaggagaat gtcaagaggc	60
gaacacacaa cgtcttgagg cgccagagga ggaacgagct aaaacggagc ttttttgccc	120
tgcgtgacca gatcccgagg ttggaaaaca atgaaaaggc cccaaggta gttatcctta	180
aaaaagccac agcatacatc ctgtccgtcc aagcagagga gcaaaagctc atttctgaag	240
aggacttggt gcggaaacga cgagaacagt tgaaacacaa acttgaacag ctacggaact	300
cttgtgcgta aggaaaagta aggaaaacga ttccttctaa cagaaatgtc ctgagcaatc	360
acctatgaac ttgtttcaaa tgcattgatca aatgcaacct cacaaccttg gctgagtc	418

<210> 103
 <211> 462
 <212> DNA
 <213> Homo Sapiens

<400> 103 aacatccgcc tggtaccag tcgctctggc tgggcacttc caccgcacc tcattcctac	60
atcaatgagt ggctccaaat agacctgggg gaggagaaga tcgtgagggg catcatcatt	120
cagggtggga agcaccgaga gaacaagggt ttcatgagga agttcaagat cgggtacagc	180
aacaacggct cggactggaa gatgatcatg gatgacagca aacgcaaggc gaagtctttt	240

36

```

gagggcaaca acaactatga tacacctgag ctgcggaactt ttccagctct ctccacgcga 300
ttcatcagga tctaccccgga gagagccact catggcggaac tggggctcag aatggagctg 360
ctgggctgtg aagtggaagc cctacagct ggaccgacca ctccaacgg gaacttggtg 420
gatgaatgtg atgacgacca ggccaactgc cacagtggaa ca 462

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<210> 104
<211> 370
<212> DNA
<213> Homo Sapiens

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<220>
<221> misc_feature
<222> (168)..(168)
<223> n is a, c, g, or t

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<400> 104
gcaaatatct taccaggcag cctatgaatt aacccaaaga agctttggtt ggttttggtg 60
gatttttatac atgccatggtt ggacatgaga ttttttagat ctctctccc acattgctag 120
acgtctcact caaagacatt tgttgggagt cacatttgca tcataganga gacagtccat 180
tcatcttagt taaattggat tgagaatgcc ttttgttcc aggaaaatat tgatcaccat 240
gaaagaagaa tagttttttt tccccagaga cattcattta gttgatataa tcctaccaga 300
aggaaagcac taagaaacac tcgtttgttg tttttaagg caacagactt aaagtgtcc 360
tcagccaagg 370

```

```

<210> 105
<211> 434
<212> DNA
<213> Homo Sapiens

```

```

<400> 105
cagggtgtatc tgcacagtgg tcgccccaca gcagaccatg tgttcacggg atgcccgcac 60
aaaacagctg aggcagctac tggagaaggt gcagaacatg tctcaatcca tagaggctctt 120
ggacaggcgg acccagagag acttgagta cgtggagaag atggagaacc aaatgaaag 180
actggagtcc aagttcaaac aggtggagga gagtcataag caacacctgg ccaggcagtt 240
taagggtctaa cttaaaagag ttttttcaat gctgcagtga ctgaagaagc agtccactcc 300
catgtaacca tgaaagagag ccagagagct ttttgacca tgcattttta ctattatttt 360
ccaatactta gcaccatttc actaaggaac cttgaatata accaggatcc tcctttgcat 420
gcgactgtag ctgc 434

```

```

<210> 106
<211> 503
<212> DNA
<213> Homo Sapiens

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<220>
<221> misc_feature
<222> (158)..(158)
<223> n is a, c, g, or t

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<220>

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<221> misc_feature
 <222> (216)..(217)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (231)..(231)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (250)..(250)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (261)..(261)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (291)..(291)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (297)..(297)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (341)..(341)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (352)..(352)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (365)..(365)
 <223> n is a, c, g, or t

<400> 106
 gcggggccaca gacgtcggaa gaaactcccg tatttgcagc tggaactgca gcccacggcg 60
 ccccggtttt cctccccgcc ctgtccctct ctggtcaaac aacatactaa agaggcgag 120
 caatgactgt tggccagttc tcaccgggga aaaaccnac tgttaggatg gcatgaacat 180
 ttcccttagat cgtggtcagc tccgaggaat gtggcnncca ggctctttga ngagccatgg 240
 gctgcaccn ggccgtaggc ntagtgtaac tcgcatccca ttgcagtgc ngtttcttg 300
 actgtgttgc tgtctcttag attaacctg ctgaggctcc nacatagctc cntggacctg 360
 tgtcttagta catactgaag cgatgggtcag agtgtgtaga gtgaagttgc tgtgccaca 420
 ttgtttgaac tcgcgtaccc cgtagataca ttgtgcaacg ttcttctgtt attcccttga 480
 ggtggtaact tcgtatgttc agt 503

<210> 107
 <211> 556
 <212> DNA
 <213> Homo Sapiens

<400> 107
 ggagacttga gcttgacctt aggatattga ttaaccactc tacagactcc cactcagtac 60

38

tgtacagggt	ggctgtggtc	ctagaagttc	agtttttact	gaggaaatat	ttccattaac	120
agcaattatt	atattgaagg	ctttaataaa	ggccacagga	gacattacta	tagcatagat	180
tgtcaaatgt	aaatttactg	agcgtgtttt	ataaaaaact	cacaggtgtt	tgaggccaaa	240
acagatttta	gacttacctt	gaacggataa	gaatctatag	ttcactgaca	cagtaaaatt	300
aactctgtgg	gtgggggagg	ggggcatagc	tctaatactaa	tatataaaat	gtgtgatgaa	360
tcaacaagat	ttccacaatt	cttctgtcaa	gcttactaca	gtgaaagaat	gggattggca	420
agtaacttct	gacttactgt	cagttgtact	tctgctccat	agacatcagt	attctgccat	480
catttttgat	gactacctca	gaacataaaa	aggaacgtat	atcacataat	tccagtcaca	540
gtttttgggt	cctctt					556

<210> 108
 <211> 543
 <212> DNA
 <213> Homo Sapiens

<400> 108						
ctgacctctt	tgaagttgca	gaatgctttg	aaattcta	aat	ggtatctgaa	atatcagctc 60
atagaaagta	acaaaatttg	ctgtcacctt	aaataagaca	ttttaatttt	gttataatgt	120
acaatttaga	agtttgatta	attatattat	ctatttaggc	attaatataa	aagaggtagg	180
agtctgttat	ttaaaaaaag	cattaaattt	aaaaaaaaac	tgtcttgtct	acttttagct	240
tcattctccc	atattttgaa	gggtgtgtaa	cttcagctct	gcaggattgc	atggggtaaa	300
acttgttacc	aacacatgtg	aaccattgct	acattgtagg	ttgtgatcat	tttgccccac	360
tgaagcccat	gtatctgacc	ttacgtgcct	tttgaactag	gagaatcggg	ctaatttatt	420
aatgatgata	attataatgt	atctgtacag	cactttttac	atttgccaag	tgctttccaa	480
tocatgttag	ttactagtta	ttacagctgt	aaggataaaa	cacgtcatgt	ggattcattt	540
tga						543

<210> 109
 <211> 458
 <212> DNA
 <213> Homo Sapiens

<400> 109						
agaaaatttg	ccaatcttct	ctactttcta	tttttatgat	gacaatcaaa	gccggcctga	60
gaaacactat	ttgtgacttt	ttaaacgatt	agtgatgtcc	ttaaaatgtg	gtctgccaat	120
ctgtacaaaa	tggctcctatt	tttgtgaaga	gggacataag	ataaaatgat	gttatacatc	180
aatatgtata	tatgtatttc	tatatagact	tggagaatac	tgccaaaaca	tttatgacaa	240
gctgtatcac	tgccctcggt	tatatTTTTT	taactgtgat	aatccccaca	ggcacattaa	300
ctgttgcaact	tttgaatgtc	caaaaatttat	atttttagaaa	taataaaaag	aaagatactt	360
acatgttccc	aaaacaatgg	tgtggtgaat	gtgtgagaaa	aactaacttg	atagggctcta	420
ccaatacaaa	atgtattacg	aatgcccttg	ttcatgtt			458

<210> 110
 <211> 412
 <212> DNA

39

<213> Homo Sapiens

<400> 110

gtcaaaccat gactcgcaca tggcaaaaga acggggccac agtacagcct cacattcttc 60
ttccaattct gaagatacag agatgtgatg aaaacaagta atagctttgg ctgtttattt 120
gatagctgtt tctgggtatt taataggaat cctttctcaa ggaatgagtt gtgacctgtt 180
tactgtctct ttagaagaaa aactccactg gaaaccattc accatgtgtg actgtcttct 240
gttatcattt gtcttacagg cggctattgc agacggctaa tttatgctta acttaggaag 300
agataaggca agagctagat ttttttcatt tgatcttttc caagcttcaa cttaacttaa 360
ctacatttct ctgtatgatg atgtctctta cttctacagg ttccttgagc ac 412

<210> 111

<211> 514

<212> DNA

<213> Homo Sapiens

<400> 111

taaattcaca tgcagtctca gagactatct agacaaagtt caagtttagga gcttttagga 60
tgtgggagta aaactttaat gggaggggag ggctggctgc tggagaagg aagaagccag 120
actggtaga cagtactctt aactcctagc ccagcctacg tgcctgccc ctctggccac 180
tgctgcagac acctgcctta acacacacac ctctaggact ccacagtttt gccttaaagg 240
accttcccaa gtctcccttt ccctgtctgg cttctccctt aagaagagag agatacttgt 300
agaattgggt ggggggaatg agcatgaact gtccttccat ttgggatatg ttacattaga 360
gtgagagaga gaataaggag cctttcttat ggaagaaatg ggagaagaga gacaggggtc 420
ttttcagcag agtctagtag tttctctgta agggaaaata atctaaaaag actaacctgc 480
ccaccactc cttatattgc tgtgagattg cccc 514

<210> 112

<211> 489

<212> DNA

<213> Homo Sapiens

<400> 112

cggaccatc caagtcactt gattgaagag catgacagaa acaaaatgta ttcaccaagc 60
attttaggat ttgacttttt cactaaccag ttgacgagca gtgcatttac aaggcactgc 120
caaacaagat gcccttgga gctgtgaggg aaagaggacc tgcgggctta gatcaatctc 180
aattcctttt catgccctcc tgcattgctg ctgcgtgggt atttgtctcc ttagccatca 240
ggtacagttt aactacaat gtaagctata ggtggagcat cagcagttag tgaggccatt 300
cttcattcctt aggatgtggc aatgaaatga tgggtgcaagt tcctttctct tttgtgaatc 360
tttcccccca ttctctgttt acatgtaacc caacaaaatg caatttctag tgccttctgt 420
ccaatcagtt ctttctctg agtgagacgt acttggtctac agatttctgc cttgttttgc 480
gacattgtc 489

<210> 113

<211> 416

<212> DNA

<213> Homo Sapiens

40

<400> 113
gattggtatg gccttagctc ttagccaaac accttcctga caccatgagg gccagcagct 60
tcttgatcgt ggtgggtgttc ctcatcgctg ggacgctggg tctagaggca gctgtcacgg 120
gagttcctgt taaagggtcaa gacactgtca aaggccgtgt tccattcaat ggacaagatc 180
ccgttaaagg acaagtttca gttaaaggtc aagataaagt caaagcgcaa gagccagtca 240
aagggtccagt ctccactaag cctgggtcct gcccattat cttgatccgg tgcgccatgt 300
tgaatcccc taaccgctgc ttgaaagata ctgactgccc aggaatcaag aagtgtgtg 360
aaggctcttg cgggatggcc tgtttcgttc ccagtgag ggagccggtc cttgct 416

<210> 114
<211> 502
<212> DNA
<213> Homo Sapiens

<400> 114
cccgaccggt gggcatttgt gaggcccatg gttgagaaat gaataatttc ccaattagga 60
agtgtaaagca gctgaggtct cttgaggag cttagccaat gtgggagcag cggtttggg 120
agcagagaca ctaacgactt cagggcaggg ctctgatatt ccatgaatgt atcaggaaat 180
atatatgtgt gtgtatgttt gcacacttgt tgtgtgggct gtgagtgtaa gtgtgagtaa 240
gagctggtgt ctgattgtta agtctaaata tttccttaa ctgtgtggac tgtgatgcc 300
cacagagtgg tctttctgga gaggttatag gtcactcctg gggcctcttg ggtccccac 360
gtgacagtgc ctgggaatgt acttattctg cagcatgacc tgtgaccagc actgtctcag 420
tttcacttcc acatagatgt ccctttcttg gccagttatc ccttcctttt agcctagtcc 480
atccaatcct cactgggtgg gg 502

<210> 115
<211> 430
<212> DNA
<213> Homo Sapiens

<400> 115
accacaacga cattgccttg ctgaagatcc gttccaagga gggcaggtgt ggcagccat 60
cccgactat acagaccatc tgcctgccct cgatgtataa cgatcccag tttggcacia 120
gctgtgagat cactggcttt ggaaaagaga attctaccga ctatctctat ccggagcagc 180
tgaagatgac tgttgtgaag ctgatttccc accgggagtg tcagcagccc cactactacg 240
gctctgaagt caccaccaa atgctgtgtg ctgctgaccc acagtggaaa acagattcct 300
gccagggaga ctgaggggga cccctcgtct gttccctcca aggccgcatg actttgactg 360
gaattgtgag ctggggcgt ggatgtgccc tgaaggacaa gccaggcgtc tacacgagag 420
tctcacactt 430

<210> 116
<211> 449
<212> DNA
<213> Homo Sapiens

<400> 116
gggttgccat ccaagtgaat gtcttttctt tgaccaaggg ggacagtcag ttttgcaaaa 60

41

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ggactctaatacctgttttaa tattgtcttc ctaattggga taatttaatt aacaagattg 120
actagaagtgaactgcaac actaacttcc ccgtgctgtg gtgtgacctg agttgggtgac 180
acaggccacagacccagag cttggcctttt gaaacacaac tcagggcctt tgtgaagggtt 240
ccccgcctga gatcttttcc cctgggttact gtgaagcctg ttggtttgct gctgtcgttt 300
ttgaggagggg cccatggggg taggagcagt tgaacctggg aacaaacctc acttgagctg 360
tgcctagaca atgtgaattc ctgtgttgct aacagaagtg gcctgtaagc tcctgtgctc 420
cggagggaag catttcctgg taggcctttg 449

```

<210> 117
 <211> 535
 <212> DNA
 <213> Homo Sapiens

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<400> 117
gctgaaggcagatgtcgtcc caaagacagc tgagaacttc agagccctgt gcaactggtga 60
gaagggttc ggctacaaag gctccacctt ccacaggggtg atcccttcc tcatgtgcc 120
ggcgggcgcac ttcaccaacc acaatggcac aggcgggaag tccatctacg gaagccgctt 180
tcctgacgag aactttacac tgaagcacgt ggggccaggt gtcctgtcca tggctaatagc 240
tggctctaac accaacggct ccagttctt catctgcacc ataaagacag actggttgg 300
tggcaagcat gttgtgttcg gtcacgtcaa agagggcatg gacgtcgtga agaaaataga 360
atctttcggc tctaagagtg ggaggacatc caagaagatt gtcacacag actgtggcca 420
gttgagctaa tctgtggcca ggggtgctggc atgggtggcag ctgcaaatgt ccatgcaccc 480
aggtggccgc gttgggctgt cagccaaggt gcctgaaacg atacgtgtgc cact 535

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<210> 118
 <211> 484
 <212> DNA
 <213> Homo Sapiens

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<400> 118
ggttgaatgt ttgtccttag gataggccta tgtgctagcc cacaaagaat attgtctcat 60
tagcctgaat gtgccataag actgacctt taaaatgttt tgagggatct gtggatgctt 120
cgtaatttg ttcagccaca atttattgag aaaatatctt gtgtcaagca ctgtgggttt 180
taatattttt aaatcaaacg ctgattacag ataatagtat ttatataaat aattgaaaaa 240
aattttcttt tgggaagagg gagaaaatga aataaatatc attaaagata actcaggaga 300
atcttcttta caattttacg tttagaatgt ttaagggtta gaaagaaata gtcaatatgc 360
ttgtataaaa cactgttcac tgtttttttt aaaaaaaaaa cttgatttgt tattaacatt 420
gatctgctga caaacctgg gaatttgggt tgtgtatgcg aatgtttcag tgcctcagac 480
aaat 484

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<210> 119
 <211> 495
 <212> DNA
 <213> Homo Sapiens

<400> 119

42

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gaacaagcgt cctggggcat ttgctattta cctggagcct tggcatttag acatctttga      60
attccttgat ttaaagaaga acacaggaaa ggaagagcag cgtgccagag atcttttctt      120
tgctcttttg attccggatc tcttcattgaa acgagtggag actaatcagg actggtcttt      180
gatgtgtcca aatgagtgtc ctggtctgga tgaggttttg ggagaggaat ttgagaaact      240
atatgcaagt tatgagaaac aaggtcgtgt ccgcaaagtt gtaaaagctc agcagctttg      300
gtatgccatc attgagtctc agacggaaac aggcaccccg tatatgctct acaaagattc      360
ctgtaatcga aagagcaacc agcagaacct gggaaccatc aaatgcagca acctgtgcac      420
agaaatagtg gagtacacca gcaaagatga ggttgctgtt tgtaatttgg ctccctggc      480
cctgaatatg tatgt                                         495

```

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<210> 120
<211> 438
<212> DNA
<213> Homo Sapiens

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<400> 120
gcccttgag tcgcgagaa agggccgtaa ccggaggacc cacgcccctg agcctcgcgc      60
tgagcggggg ccgcgcagcg caacgcactg gtgaccagac tgtcccacg ccgggaacca      120
agcaggagac gacaggcgag agaggagcca gacagacct gaaaagaagg acgggttggg      180
gccgggcaca ttgggggtca ccggccgatg gagacaccaa ccgacaggcc ctggctgagg      240
gcagctgcgc gggcttattt attaacagga taacccttga atgtagcagc cccgggaggg      300
cggcacaggt cgggcgcagg attcagccgg agggaaggga cggggaagcc gagctccaga      360
gcaacgacca gggccgagga ggtgcctgga gtgcccaccc tgggagacag accccacctc      420
cttgggtagt gagcagtg                                         438

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```

<210> 121
<211> 447
<212> DNA
<213> Homo Sapiens

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<220>
<221> misc_feature
<222> (116)..(116)
<223> n is a, c, g, or t

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<220>
<221> misc_feature
<222> (362)..(362)
<223> n is a, c, g, or t

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<400> 121
ggaactacgg ggcttacagg agcttttgtg tgcttggttag aaactatttc tgttccagtc      60
acattgccat cactcttgta ctgcctgcc cgcgggagga ggctggtgac aggccnaaag      120
gccagtggaa gaaacaccct ttcattctag agtccactgt ggcactggcc acccctcccc      180
agtacagggg tgctgcaggt ggcagagtga atgtcccca tcatgtggcc caactctcct      240
ggcctggcca tctccctccc cagaaacagt gtgcatgggt tattttggag tgtaggtgac      300
ttgtttactc attgaagcag atttctgctt ctttttattt ttataggaat agaggaagaa      360
angtcagatg cgtgccacgc tcttcacccc ccaatctctt ggtggggagg ggtgtaccta      420

```

aatattttatc atatccttgc ccttgag

447

<210> 122
 <211> 323
 <212> DNA
 <213> Homo Sapiens

<400> 122
 aaattgacca tacaatttca tcctccttca ggggatcaaa aggacggagt ggggggacag 60
 agactcagat gaggacagag tggtttccaa tgtgttcaat agatttagga gcagaaatgc 120
 aaggggctgc atgacctacc aggacagaac tttccccaat tacagggtga ctcacagccg 180
 cattggtgac tcacttcaat gtgtcatttc cggctgctgt gtgtgagcag tggacacgtg 240
 aggggggggt gggtagagaga gacaggcagc tcggattcaa ctaccttaga taatatttct 300
 gaaaacctac cagccagagg gta 323

<210> 123
 <211> 499
 <212> DNA
 <213> Homo Sapiens

<400> 123
 gtatcaggct tcaattccat tatgttttaa tgttgtctct gaagatgact tgtgattttt 60
 ttttcttttt tttaaaccat gaagagccgt ttgacagagc atgctctgcg ttgttggttt 120
 caccagcttc tgccctcaca tgcacaggga tttacaaca aaaatataac tacaacttcc 180
 cttgtagtct cttatataag tagagtcctt ggtactctgc cctcctgtca gtagtggcag 240
 gatctattgg catattcggg agcttcttag agggatgagg ttctttgaac acagtgaaaa 300
 tttaaattag taactttttt gcaagcagtt tattgactgt tattgctaag aagaagtaag 360
 aaagaaaaag cctgttgga atcttggtta tttctttaag atttctggca gtgtgggatg 420
 gatgaatgaa gtggaatgtg aactttgggc aagttaaag ggacagcctt ccatgttcat 480
 ttgtctacct ctttaactga 499

<210> 124
 <211> 328
 <212> DNA
 <213> Homo Sapiens

<400> 124
 taattttaga ttcgccttac aatgtaaac ttcacattgg agataatatt ggttggacct 60
 tgcccatctt cactctagcc ttcgtatttg tgaaggactc agccaccttc cttcttcacc 120
 ccatgcttct caccaaattt ttgttgtcat tgagggcact tggataactc aagttgatat 180
 ttatagctga tcaatctata tgtgtcacag aactatgtg cctaaagtga tcttggctcc 240
 ttaatggtcc ttttggcccc ttggatagtt aacagctgag taattctaatt ctcttctgtg 300
 ttttccttgc ctttaaccaca aattgtgg 328

<210> 125
 <211> 489
 <212> DNA
 <213> Homo Sapiens

44

<400> 125
gagatacaga acttggtgac ccatgtattg cataagctaa agcaacacag acactcctag 60
gcaaagtttt tgtttgtgaa tagtacttgc aaaacttgta aattagcaga tgactttttt 120
ccattgtttt ctccagagag aatgtgctat atttttgtat atacaataat atttgcaact 180
gtgaaaaaca agttgtgcc a tactacatgg cacagacaca aaatattata ctaatatgtt 240
gtacattcgg aagaatgtga atcaatcagt atgttttttag attgtatttt gccttacaga 300
aagcctttat tgtaagaactc tgatttcctt ttggacttca tgtatattgt acagttacag 360
taaaattcaa cctttatttt ctaatttttt caacatattg tttagtgtaa agaataattta 420
tttgaagttt tattatttta taaaaaagaa tattttattt aagaggcatc ttacaaattt 480
tgccccctt 489

<210> 126
<211> 503
<212> DNA
<213> Homo Sapiens

<400> 126
gcggcatgtg accatcattg aactggtggg acagccacct caggagggtg ggcgcatccg 60
ggagcaacag ctgtcagcca acatcatcga ggagctcagg caatttcagc gcctcactcg 120
ctcctacttc aacatggtgt tgattgacaa gcagggtatt gaccgagacc gctacatgga 180
acctgtcacc ccgaggaaa tcttcacatt cattgatgac tacctactga gcaatcagga 240
gttgaccag cgctgggagc aaagggacat atgcgagtga acttgagcca gggcatgggt 300
aaagtcaagg gaaaagctcc tctagttagc tgaaactggg acctaatata aggaggaaat 360
gttttccac agttctaggg acaggactct gaggtgggtg agtttgacaa atcctgcagt 420
gtttccaggc atccttttag gactgtgtaa tagtttcctt agaagctagg tagggactga 480
ggacaggcct tgggcagtgg gtt 503

<210> 127
<211> 436
<212> DNA
<213> Homo Sapiens

<400> 127
agactgggcg aaaggctgtc cggagggcag accagggtgc ttgccgcaga gaaaacacca 60
aagtctcctg ttcgctcata aagaagtttt tgggatggga gagaatccag accatcttgg 120
ggcagccagg cccttgccct catTTTTTaca gaggtagcac aactgattcc aacacaaaac 180
cccttcccct ttttaaaatg atttctgttc taatgccata gatcaaaggc ctcagaaacc 240
attgtgtgtt tcctctttga agcaatgaca agcactttac tttcacgggtg gtttttgttt 300
tttcttattg ctgtggaacc tcttttgag gacgttaaag gcgtgtttta cttgtttttt 360
taagagtgtg tgatgtgtgt tttgtagatt tcttgacagt gctgtaatac agacggcaat 420
gcaatagcct atttaa 436

<210> 128
<211> 497
<212> DNA
<213> Homo Sapiens

45

<400> 128
 cctgccctct agttgggtct gggctttgat ctcttccaac ctgccagtc acagaaggag 60
 gaatgactca aatgccc aaa accaagaaca cattgcagaa gtaagacaaa catgtatatt 120
 tttaaagtgt ctaacataag acctgttctc tctagccatt gatttaccag gctttctgaa 180
 agatctagtgt gttcacacag agagagagag agtactgaaa aagcaactcc tcttcttagt 240
 cttaataatt tactaaaatg gtcaactttt cattatcttt attataataa acctgatgct 300
 tttttttaga actccttact ctgatgtctg tatatgttgc actgaaaagg ttaatatatta 360
 atgttttaaat ttattttgtg tggtaagtta attttgattt ctgtaatgtg ttaatgtgat 420
 tagcagttat tttccttaat atctgaatta tacttaaaga gtagtgagca atataagacg 480
 caattgtgtt tttcagt 497

<210> 129
 <211> 321
 <212> DNA
 <213> Homo Sapiens

<400> 129
 gtttggtatgg tgggaaggctct cattttattg agatttttaa gatacatgca aaggtttggg 60
 aatagaacct ctaggcaccc tcctcagtgt ggggtggctg agagttaaag acagtgtggc 120
 tgcagtagca tagaggcgcc tagaaattcc acctgcaccg tagggcatgc tgataccatc 180
 ccaatagctg ttgccattg acctctagtgt gtgagtttct agaatactgg tccattcatg 240
 agatattcaa gattcaagag tattctcact tctgggttat cagcataaac tgggaatgtag 300
 tgtcagagga tactgtggct t 321

<210> 130
 <211> 553
 <212> DNA
 <213> Homo Sapiens

<400> 130
 tttgctgca gtttcttgtg tagatttgaa aattgtatac caatgtgttt tctgtagact 60
 ctaagataca ctgcactttg tttagaaaaa aaactgaaga tgaaatatat attgtaaaga 120
 agggatatta agaacttag ataacttctt gaaaaagatg gcttatgtca tcagtaaagt 180
 acctttatgt tatgaggata taatgtgtgc tttattgaat tagaaaatta gtgaccatta 240
 ttcacagggtg gacaaatgtt gtcctgttaa tttataggag ttttttgggg atgtggaggt 300
 agttgggtag aaaaattatt agaacattca cttttgttaa cagtatttct cttttattct 360
 gttatatagt ggatgatata cacagtggca aaacaaaagt acattgctta aaatatatag 420
 tgaaaaatgt cactatatct tcccatttaa cattgttttt gtatattggg tgtagatttc 480
 tgacatcaaa acctggaccc ttggaaaaca aaagttttta ttaaaaaaaa tccttgtgac 540
 ttacaatttg cac 553

<210> 131
 <211> 419
 <212> DNA
 <213> Homo Sapiens

46

<400> 131
gagtcggaga tgatgcagca cacacacaat tccccagccc agtgatgctt gtgttgacca 60
gatgttcctg agtctggagc aagcaccag gccagaataa cagagcttcc ttagttggtg 120
aagacttaaa catctgcctg aggtcaggag gcaatttgcc tgccttgtag aaaagctcag 180
gtgaaagact gagatgaatg tctttcctct cctgcctcc caccagactt cctcctggaa 240
aacgcttttg tagatttggc caggagcttt cttttatgta aattggataa atacacacac 300
catacactat ccacagatat agccaagtag atttggttag aggatactat ttccagaata 360
gtgttttagct cacctagggg gatatgtttg tatacacatt tgcataacc cacatgggg 419

<210> 132
<211> 414
<212> DNA
<213> Homo Sapiens

<400> 132
ttgttgctgt tgcttggttg aagaaaatca tgacattcca agttgacatt ttttttttca 60
ttttaattaa aatttgaaat tctgaacacc gtcagcacc tctcttccct atcatgggtc 120
atctgacccc tgcctgtctc cttgtccctg cttcatgttt gggggccttt ctttaactgc 180
cttctctggct tagctcagat ggcagatgag agtgtagtca agggcctggg cacaggaggg 240
agagctgcag agtgctcctgc ctgccttggc tggagggaca cctctcctgg gtgtggagac 300
agcttggttc cctttcccta gctccctggt ggggtgaatgc cacctcctga gatcctcacc 360
tcttggaatt aaaattgttg gtcactgggg aaagcctgag tttgcaacca gttg 414

<210> 133
<211> 419
<212> DNA
<213> Homo Sapiens

<400> 133
aggggctgaa ctatcggtat cacctgggtt gtaactgcaa gatcaagtcc tgctactacc 60
tgcttgctt tgtagacttcc aagaacgagt gtctctggac cgacatgctc tccaatttcg 120
gttaccctgg ctaccagtcc aaacactacg cctgcatccg gcagaagggc ggctactgca 180
gctggtaccg aggatgggccc cccccgata aaagcatcat caatgccaca gacccctgag 240
cgccagaccc tgccccacct cacttccctc ccttcccgct gagcttccct tggacactaa 300
ctcttcccag atgatgacaa tgaaattagt gcctgttttc ttgcaaattt agcacttgga 360
acattttaaag aaaggtctat gctgtcatat ggggtttatt gggaactatc ctctgggc 419

<210> 134
<211> 493
<212> DNA
<213> Homo Sapiens

<400> 134
gacttttttg aatagccctg tctagggcaa actgtggccc ccaggagaca ctacccttcc 60
atgccccaga cctctgtctt gcatgtgaca attgacaatc tggactacco caagatggca 120
cccaagtgtt tggottcttg ctacctaaagg ttaacatgtc actagagtat ttttatgaga 180
gacaaacatt ataaaaatct gatggcaaaa gcaaaacaaa atggaaagta ggggaggtgg 240

47

```

atgtgacaac aacttccaaa ttggctcttt ggagggcgaga ggaaggggag aacttggaga    300
atagtttttg ctttgggggt agaggcttct tagattctcc cagcatccgc ctttcccttt    360
agccagtctg ctgtcctgaa acccagaagt gatggagaga aaccaacaag agatctcgaa    420
ccctgtctag aaggaatgta tttgttgcta aatttcgtag cactgtttac agttttcctc    480
catgttattt atg                                                    493

```

```

<210> 135
<211> 567
<212> DNA
<213> Homo Sapiens

```

```

<400> 135
gagtattact agagctttgc cacctctcca tttttgcctt ggtgctcatc ttaatggcct    60
aatgcacccc caaacatgga aatatcacca aaaaatactt aatagtcac caaaaggcaa    120
gactgccctt agaaattcta gcctggtttg gagatactaa ctgctctcag agaaagtagc    180
tttgtgacat gtcatgaacc catgtttgca atcaaagatg ataaaataga ttcttatttt    240
tccccacccc ccgaaaatgt tcaataatgt cccatgtaaa acctgctaca aatggcagct    300
tatacatagc aatggtaaaa tcatcatctg gatttaggaa ttgctcttgt cataccccc    360
agtttctaag atttaagatt ctcttacta ctatcctacg tttaaatata ttgaaagtt    420
tgtattaaat gtgaatttta agaaataata tttatatttc tgtaaatagta aactgtgaag    480
atagttataa actgaagcag atacctggaa ccacctaaag aacttcatt tatggaggat    540
ttttttgccc cttgtgtttg gaattat                                                    567

```

```

<210> 136
<211> 479
<212> DNA
<213> Homo Sapiens

```

```

<220>
<221> misc_feature
<222> (441)..(441)
<223> n is a, c, g, or t

```

```

<400> 136
accaaggttc tcatgaatct ccaaccttaa atcctgaaac agtggcaata aatttatctg    60
atgttgactt gagtaaatat atcaccacta ttgctggagt catgacacta agtcaagtta    120
aaggctttgt tcgaaagaat ggtgtcaatg aagccaaaat agatgagatc aagaatgaca    180
atgtccaaga cacagcagaa cagaaagttc aactgcttcg taattggcat caacttcag    240
gaaagaaaga agcgtatgac acattgatta aagatctcaa aaaagccaat ctttgtactc    300
ttgcagagaa aattcagact atcatcctca aggacattac tagtgactca gaaaattcaa    360
acttcagaaa tgaaatccaa agcttggctc agagtgaata acaacaaatt cagttctgag    420
tatatgcaat tagtgtttga naagattctt aatagctggc tgtaaatact gcttggttt    479

```

```

<210> 137
<211> 490
<212> DNA
<213> Homo Sapiens

```


48

<400> 137
gtagcagctc acataactgg gaccagagga agaagcaaca cattgtcttc tccaaactcc 60
aagaatgaaa aggctctggg ccgcaaaata aactcctggg aatcatcaag gagtgggcat 120
tcattcctga gcaacttgca cttgaggaat ggtgaactgg tcatccatga aaaagggttt 180
tactacatct attcccaaac atactttcga tttcaggagg aaataaaaga aaacacaaag 240
aacgacaaac aaatgggtcca atatatttac aaatacacia gttatcctga ccctatattg 300
ttgatgaaaa gtgctagaaa tagttgttgg tctaaagatg cagaatatgg actctattcc 360
atctatcaag ggggaatatt tgagcttaag gaaaatgaca gaatttttgt ttctgtaaca 420
aatgagcact tgatagacat ggaccatgaa gccagttttt tcggggcctt tttagttggc 480
taactgacct 490

<210> 138
<211> 248
<212> DNA
<213> Homo Sapiens

<400> 138
ctctacctca tatcagtttg ctagcagaaa tctagaagac tgtcagcttc caaacattaa 60
tgcaatgggt aacatcttct gtctttataa tctactcctt gtaaagactg tagaagaaag 120
cgcaacaatc catctctcaa gtagtgtatc acagtagtag cctccagggt tccttaaggg 180
acaacatcct taagtcaaaa gagagaagag gcaccactaa aagatcgag tttgcctggt 240
gcagtggc 248

<210> 139
<211> 405
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (64)..(64)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (68)..(68)
<223> n is a, c, g, or t

<400> 139
gctcaccag cagatgttcg atgccaagaa catgatggcc gcctgcgacc cgcgccacgg 60
ccgnetanct gacggtggcc accgtgttcc ggggccgcat gtccatgaag gaggtggacg 120
agcagatgct ggccatccag agcaagaaca gcagctactt cgtggagtgg atccccaaca 180
acgtgaaggt ggccgtgtgt gacatccgc cccgcggcct caagatgtcc tccaccttca 240
tcgggaacag cacgyccatc caggagtgtt tcaagcgcat ctccgagcag ttcacggcca 300
tgttccggcg caaggccttc ctgcactggt acacgggcga gggcatggac gagatggagt 360
tcaccgaggc cgagagcaac atgaacgacc tgggtgtccga gtacc 405

<210> 140
<211> 407
<212> DNA

<213> Homo Sapiens

<400> 140

```

gatgcctaac caaggactag agctccttct tgagatctaa atctaaagta aatgtgcatt      60
aaagcagtggt gcttcaaagg catcagacga tgaaagcaac ataccacaac taggagttat      120
ttctcaaaact taaatgtcct ctgggaatcc agacttaaaa ataagagcaa acttaacaca      180
ctatccattt tcgagcaaac ttaaccact atattccattt tgcctcatgtg ttttatgcaa      240
ccagctttcc atcaaatcct caatccttga atccaggtaa aagggttaatt atcctaggtat      300
tagtgaatga ttcaatgaag ctttcttgaa aacaaacata ggagtgtaat gtactattat      360
gtttgtatcc tgttttagtt tataaagcac ttccacatac attatgg                      407

```

<210> 141

<211> 518

<212> DNA

<213> Homo Sapiens

<400> 141

```

accaactac tctggtacca ttgctttggc cctgtagtg tgccttggtg gaggtttgct      60
ttatttgaga aggaacaact tggagttcat ctataacaag actggttggg ccatggtgtc      120
tctgtgtata gtctttgcta tgacttctgg ccagatgtgg aaccatatcc gtggacctcc      180
atatgtctcat aagaaccac acaatggaca agtgagctac attcatggga gcagccaggc      240
tcagtttgtg gcagaatcac acattattct ggtactgaat gccgctatca ccatggggat      300
ggttcttcta aatgaagcag caacttcgaa aggcgatgtt ggaaaaagac ggataatttg      360
cctagtggga ttgggcctgg tggcttctct ctacagtttt ctactttcaa tatttcgttc      420
caagtaccac ggctatcctt atagtgatct ggactttgag tgagaagatg tgatttggac      480
catggcactt aaaaactcta taacctcagc cttttaat                             518

```

<210> 142

<211> 443

<212> DNA

<213> Homo Sapiens

<400> 142

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ctttgctatg acttctggcc agatgtggaa ccatatccgt ggacctccat atgctcataa      60
gaaccacac aatggacaag tgagctacat tcatgggagc agccaggctc agtttgtggc      120
agaatcacac attattctgg tactgaatgc cgctatcacc atggggatgg ttcttctaaa      180
tgaagcagca acttcgaaag gcgatgttg aaaaagacgg ataatttgcc tagtgggatt      240
gggcctgggt gtcttcttct tcagttttct actttcaata tttcgttcca agtaccacgg      300
ctatccttat agctttttta ttaaatgaag ccaagtggga ttgcataaa gtgaatgttt      360
accatgaaga taaactgttc ctgactttat actattttga attcattcat ttcattgtga      420
tcagctagct tattcttgtg tac                                              443

```